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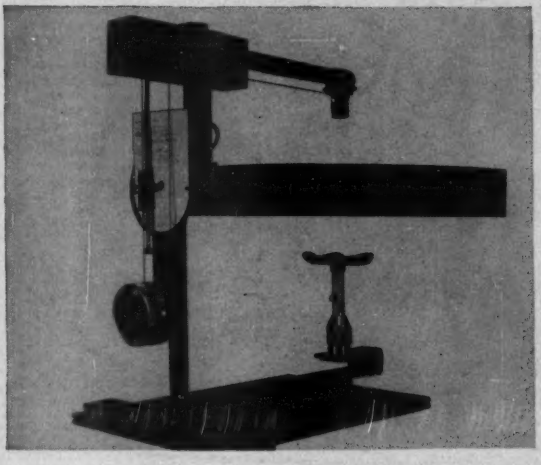

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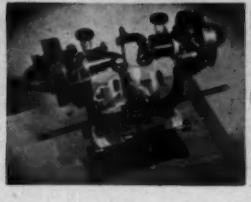

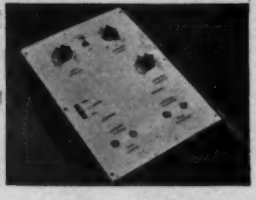

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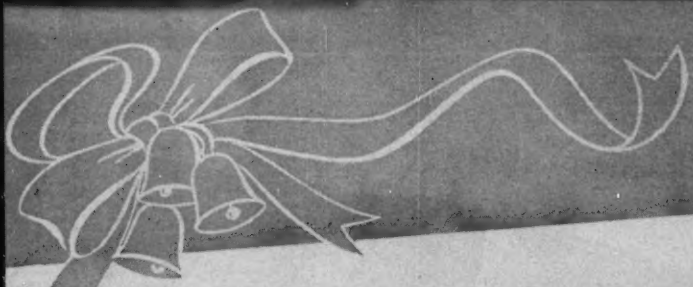

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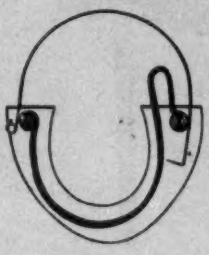

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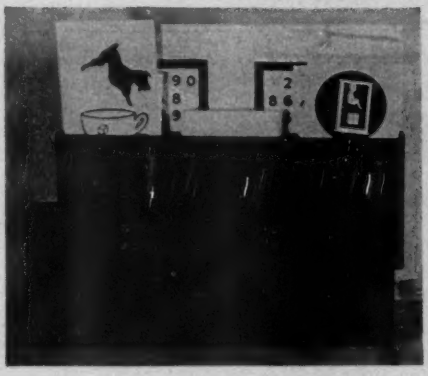

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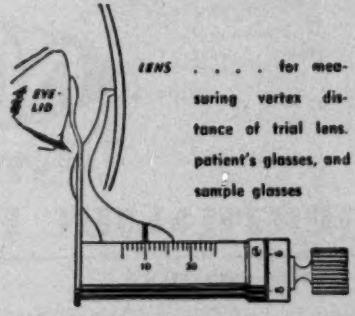

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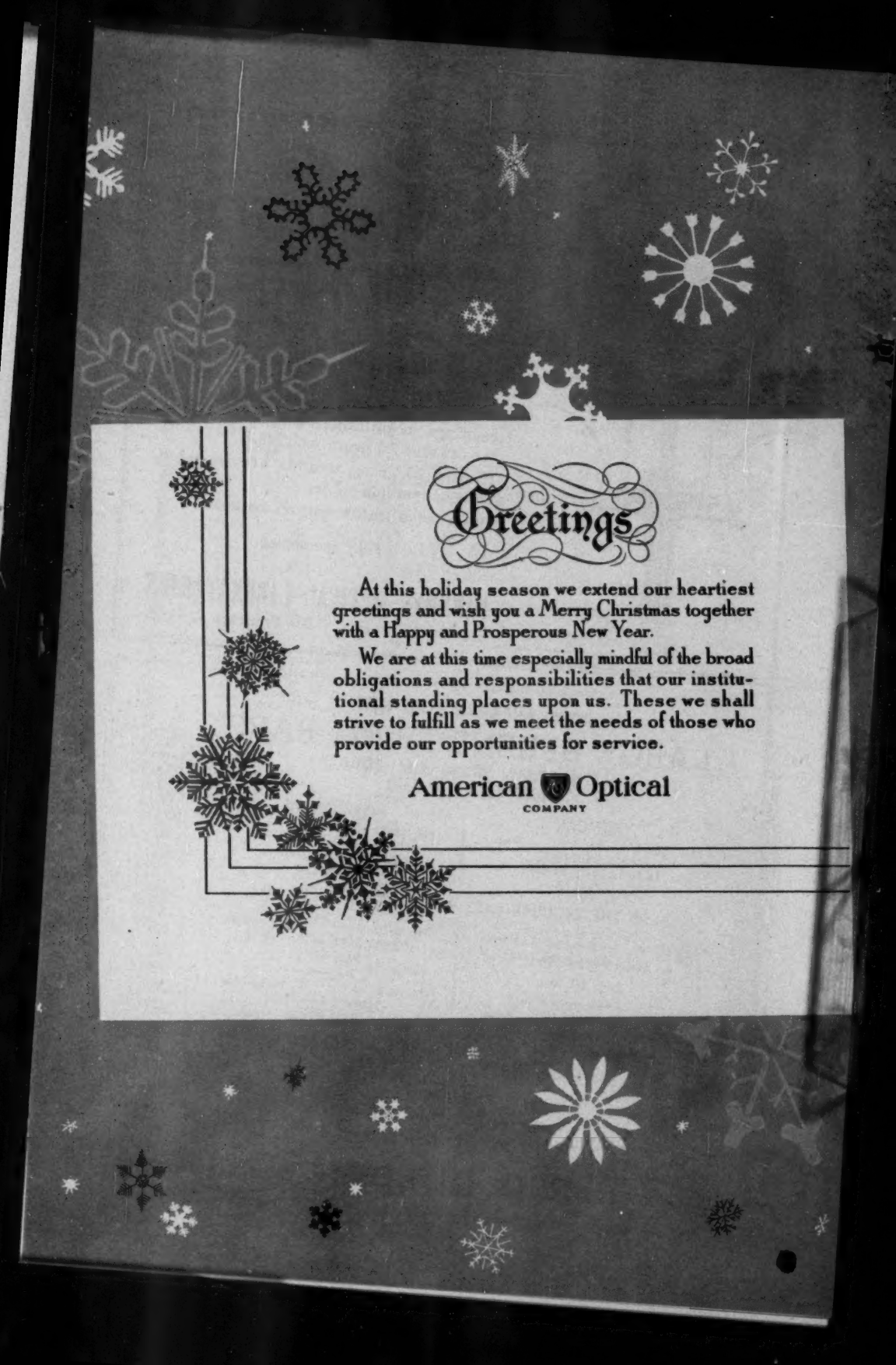

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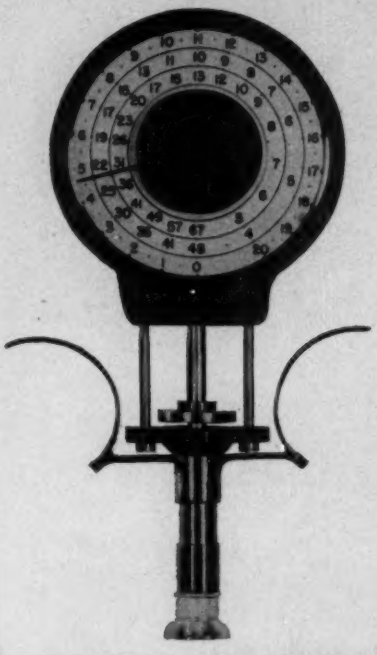

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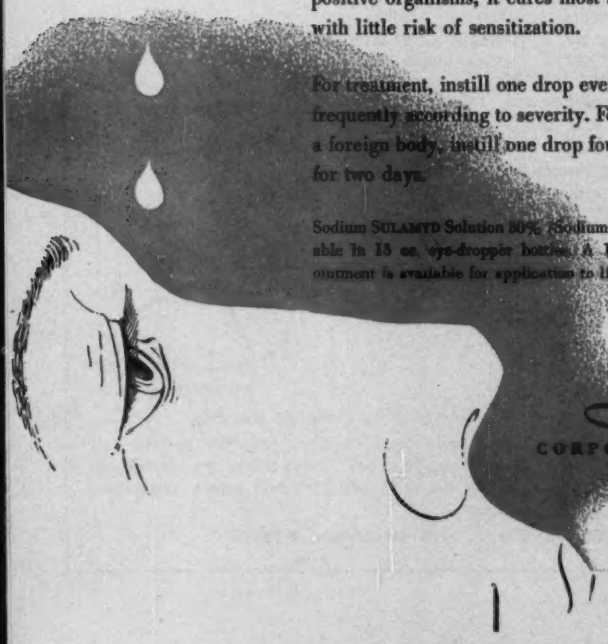

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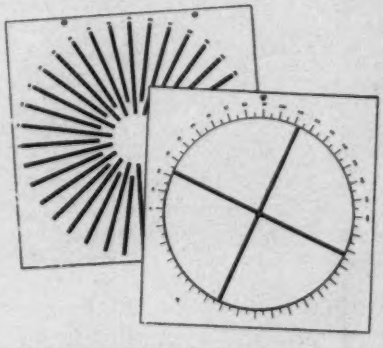

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ANTICOAGULANT THERAPY IN OCCLUSIVE VASCULAR DISEASE OF THE RETINA

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SINCE anticoagulant therapy of occlusive vascular diseases of the retina is rapidly assuming an important place in the armamentarium of the ophthalmologist, it is important that we review the efficiency, as well as the dangers and contraindications, of this form of treatment. It is the purpose of this paper to analyze the results of bishydroxycoumarin U. S. P. (dicumarol®) and heparin therapy in the management of occlusive vascular disease of the retina at the University Hospital during the past few years. We have attempted to establish a control for the present study by reviewing the end-results in all untreated patients seen here since 1935.

The accumulated experience of the world literature [1] with anticoagulant drugs in treatment of thrombosis of the retinal veins has been summarized in Tables 1,

Read before the Section on Ophthalmology at the One-Hundredth Annual Session of the American Medical Association, Atlantic City, N. J., June 15, 1951.

From the Departments of Ophthalmology (Dr. Falls) and Internal Medicine (Drs. Duff and Linman), University of Michigan Medical School, and University Hospital.

1. (*a*) Holmin, N., and Ploman, K. G.: Thrombosis of Central Vein of Retina Treated with Heparin, Lancet **1**:664 (March 19) 1938. (*b*) MacDonald, A. E.: Heparin in Thrombosis of the Central Vein, Tr. Am. Ophth. Soc. **38**:313, 1940. (*c*) Heath, P., in discussion on MacDonald.[1b] (*d*) Klien, B. A.: Anticoagulant Therapy of Occlusion of Central Vein of Retina in Relation to Pathogenesis and Differential Diagnosis, Arch. Ophth. **29**:699 (May) 1943. (*e*) Boström, C. G., and William-Olsson, L.: Thrombosis of Central Vein of Retina Successfully Treated with Heparin: A Second Case, Lancet **2**:78 (July 9) 1938. (*f*) Rea, R. L.: Treatment of Thrombosis in the Central Vein of the Retina by Heparin, Tr. Ophth. Soc. U. Kingdom **60**:213, 1940. (*g*) Ellison, J., in discussion on Rea.[1f] (*h*) Benedict, W. L., and Wagener, H. P.: Treatment of Thrombosis of the Retinal Veins, Am. J. M. Sc. **202**:306 (Feb.) 1941. (*i*) Huggett, A. St. G., and Juler, F. A.: Heparin in Thrombosis of the Central Vein of the Retina, Tr. Ophth. Soc. U. Kingdom **62**:123, 1942. (*j*) Kravitz, D.: Heparin in the Treatment of Thrombosis of the Central Retinal Vein or of Its Branches, Am. J. Ophth. **25**:1367 (Nov.) 1942. (*k*) Levison, L. A., and Roberts, J. L.: Heparin Therapy in Thrombosis of the Central Vein of the Retina, Ohio M. J. **38**:338 (April) 1942. (*l*) Rychener, R. O.: Use of Heparin in Treatment of Thrombosis of the Central Vein of the Retina, South. M. J. **35**:652 (July) 1942. (*m*) Benz, A. H., and Lemoine, A. N., in discussion on Rychener.[1l] (*n*) Rosenthal, C. M., and Guzek, J. T.: Thrombosis of Central Retinal Vein Treated Successfully with Heparin: Two Cases, Arch. Ophth. **30**:232 (Aug.) 1943. (*o*) Palomar Palomar, A.: La medicación anticoagulante (heparina, dicumarol) en el tratamiento de las trombosis de las venas retinianas, Arch. Soc. oftal. hispano-am. **7**:247 (March) 1947. (*p*) Moréu, in discussion on Palomar.[1o] (*q*) Qvist, A.:

(Footnote continued on next page)

2, and 3. Since patients with secondary glaucoma were excluded from treatment, the material is admittedly selective. Of 109 patients with thrombosis of the central retinal vein who were treated with heparin, the condition of 59% appears to have improved; that of 15% was unchanged, and that of 27% had grown worse; 12% had glaucoma, and 6% of the eyes required enucleation. For those who improved (Table 2), the average initial visual acuity was 0.25, and the final vision was 0.60. Of 84 patients with thrombosis of a tributary retinal vein treated with heparin, the condition of 59% had improved, that of 24% was unchanged, that of 17% had grown worse; only 2.3% had glaucoma, while only one eye required enucleation. For patients who showed improvement, the initial visual acuity averaged 0.33, and the final vision was 0.68.

Of 23 patients with thrombosis of the central retinal vein treated with bishydroxycoumarin (Table 1), the condition of 70% appears to have improved; that of 26% was unchanged; that of only one had grown worse; none of the eyes became glaucomatous or required enucleation. For 10 patients who improved (Table 3) the visual acuity was 0.33 before, and 0.76 after, treatment. Eight of 11 patients with thrombosis of tributary retinal veins showed improvement when treated with bishydroxycoumarin, while the condition of 3 became worse. For six of the patients who showed improvement, the initial vision averaged 0.18; it was 0.68 at the termination of treatment. Rosengren [1d'] administered bishydroxycoumarin to 32 patients with retinal-vein thrombosis an average of 24 days, with a control examination one month later. The mean value for vision was 0.22 before treatment and 0.36 after treatment. Secondary glaucoma developed in 1 of 20 patients with central-vein thrombosis who was treated with bishydroxycoumarin.

Ploman [1r] has concluded that of 38 patients with thrombosis of the central retinal vein who were treated with heparin, somewhat more than 25% escaped without ill effect; 52% retained their reading faculty; 16% could see to walk, and 31% became blind. Of 31 patients with tributary-vein thrombosis treated with heparin, vision was completely restored in 29%; 48% could read; 45% could see

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TABLE 1.—*Course in Collected Cases of Retinal-Vein Thrombosis Treated with Anticoagulants*

Type	No. of Cases	Visual Acuity			Glaucoma	Enucleation
		Improved *	Unchanged	Worse		
Heparin						
Central retinal vein †	109	64 (59%)	16 (15%)	29 (27%)	13 (12%)	7 (6%)
Retinal tributary vein ‡	84	50 (59%)	20 (24%)	14 (17%)	2 (2.3%)	1 (1.0%)
Dicumarol®						
Central retinal vein §	23	16 (70%)	6 (26%)	1 (4%)	0	0
Retinal tributary vein ‖	11	8 (73%)	0	3 (27%)	0	0

* Demonstrating an increase of at least 0.1 in visual acuity.

† Holmin and Ploman.[1a] MacDonald.[1b] Klien.[1d] Heath.[1c] Boström and William-Olsson.[1e]

‡ MacDonald.[1b] Heath.[1c] Boström and William-Olsson.[1e] Rea.[1f] Ellison.[1g]

§ Klien.[1d] Palomar.[1e] Moréu.[1p] Blum and Jeanneret.[1s'] MacLean and Brambel.[1b'] Banks-Smith.[1c'] Rosengren.[1d'-f']

‖ Palomar.[1e] Moréu.[1p] Blum and Jeanneret.[1s'] MacLean and Brambel.[1b'] Rosengren.[1d'-f']

TABLE 2.—*Visual Acuity in Collected Cases of Retinal-Vein Thrombosis Treated with Heparin*

Source	No. of Cases	Vision Improved	Average Initial Visual Acuity	Final Visual Acuity	Observation Period	Visual Acuity Unchanged	Visual Acuity Worse	Glaucoma	Enucleations
Central Retinal Vein									
Ploman [1r]	38	21	0.3	0.8	2.1 yr.	4	13	8	4
Rosengren and Stenström [1t]	10	3	0.08	0.28	1 mo.	3	4	0	..
Larsson [1u]	7	7	0.47	1.0	12-44 mo.	..	..	..	..
Mählén [1v]	10	8	....	0.44	1 yr.	1	1	0	..
Ciotola [1w]	16	9	0.16	0.49	10 days	3	4	1	1
Total	81	48	0.25	0.60	.....	11	22	9	5
Retinal Tributary Vein									
Ploman [1r]	31	14	0.4	0.8	2.5 yr.	12	5	1	1
Rosengren [1s]	20	8	0.18	0.61	1 mo.	9	3	0	..
Mählén [1v]	7	6	....	0.6	1 yr.	0	1	0	0
Ciotola [1w]	19	16	0.42	0.89	10 days	1	2	0	0
Total	77	44	0.33	0.68	.....	22	11	1	1

TABLE 3.—*Visual Acuity in Collected Cases of Retinal-Vein Thrombosis Treated with Dicumarol®*

Source	No. of Cases	Vision Improved	Average Initial Visual Acuity	Final Visual Acuity	Observation Period	Vision Unchanged	Vision Worse	Glaucoma	Enucleation
Central Retinal Vein									
Blum and Jeanneret [1s']	6	5	0.25	0.64	10 days-2 mo.	..	1	..	..
MacLean and Brambel [1b']	5	4	0.13	0.55	Months	1	..	..	..
Banks-Smith [1c']	1	1	0.60	1.00	2 mo.	..	..	..	..
Total	12	10	0.33	0.76	.....	1	1	..	..
Retinal Tributary Vein									
Palomar [1e]	6	3	0.20	0.90	3 mo.	..	3	..	..
Blum and Jeanneret [1s']	1	1	0.10	0.50	2 mo.	..	..	..	..
MacLean and Brambel [1b']	2	2	0.25	0.65	Months	..	..	..	..
Total	9	6	0.18	0.68	.....	..	3	..	..

to walk, and 6% became blind. He emphasized the extent of retinal abnormalities persisting despite treatment. Of 20 patients with central-vein thrombosis who escaped without ill effect, 14 presented normal fundi, while chorioretinitis developed in 6. Of the group with tributary-vein thrombosis, persistent vascular lesions of some sort were observed in all.

Klien [1d] has emphasized that anticoagulant therapy may be of no benefit in occlusion of the central retinal vein of arteriosclerotic or inflammatory origin. Verhoeff [2] has repeatedly insisted that occlusion of the central retinal vein is usually secondary to endophlebitis; in cases of this type he is pessimistic about the chances for successful anticoagulant therapy. Huggett and Juler [11] reported mediocre results from anticoagulant therapy. Jensen [3] reported a case of occlusion of the central retinal vein which developed during treatment of coronary thrombosis with anticoagulants. Brændstrup [4] concluded that "it has not, as yet, been possible to offer an efficient therapy for central vein thrombosis." He adopted a negative attitude toward the application of anticoagulant drugs and stressed the seriousness of their complications for the patient, as well as for the physician.

Heparin and bishydroxycoumarin have been employed in treatment of a limited number of patients with other types of retinal abnormalities, including retinal-artery occlusion,[5] hypertensive and arteriosclerotic retinopathy,[6] serous (angiospastic) retinopathy,[1b'] diabetic retinopathy,[6a,b] vitreous [1q,r] and choroidal hemorrhage, glaucomatous optic nerve atrophy,[7] and uveitis.[8]

COURSE IN UNTREATED OCCLUSIVE VASCULAR DISEASE OF THE RETINA

Only a few reports are available which are adequate for evaluating the natural course of untreated occlusive vascular disease of the retina. Moore's [9] excellent monograph stressed the unfavorable end-result of untreated retinal-vein occlusion. McLean [10] reported that only 1 of 18 eyes presenting occlusion of the central retinal vein achieved better than 6/60 vision. Duke-Elder [11] noted that the resultant visual acuity is generally poor, especially when the macular area is involved. Odqvist [12] was the first author, using a large series of cases, to report a fairly

2. Verhoeff, F. H.: Obstruction of the Central Retinal Vein, Arch. Ophth. **36**:1, 1907.

3. Jensen, J. P.: Centralvenetrombose i retina opstået under dikumarolbehandling, Nord. med. **43**:996, 1950.

4. Brændstrup, P.: Central Retinal Vein Thrombosis and Hemorrhagic Glaucoma, Acta ophth., Supp. 35, 1950.

5. (*a*) Arkle, J. S.: Retinal Artery Thrombosis Treated by Heparin, Tr. Ophth. Soc. U. Kingdom (Pt. II) **59**:422, 1939. (*b*) Girault-Dangely, Y.: Antivitamine K et oblitération de l'artère centrale de la retiné, Presse méd. **53**:327 (June 16) 1945. (*c*) MacDonald.[1b] (*d*) Rychener.[11] (*e*) Qvist.[1q] (*f*) MacRae.[1y] (*g*) Blum and Jeanneret.[1a']

6. (*a*) Larsson.[1q] (*b*) MacLean and Brambel.[1b'] (*c*) Girault-Dangely.[5b]

7. McGuire, W. P.: The Effect of Dicumarol on the Visual Fields in Glaucoma: A Preliminary Report, Am. J. Ophth. **32**:1095 (Aug.) 1949.

8. Bick, M. W., and Wood, R. M.: Heparin and Uveitis, Am. J. Ophth. **12**:1878 (Dec.) 1950. Steffensen, E. F.: Personal communication to the authors.

9. Moore, R. F.: Retinal Venous Thrombosis, London, G. P. Putnam's Sons, 1924.

10. McLean, J. M.: Anticoagulant Therapy in Retinal Vascular Occlusion, Tr. Am. Acad. Ophth. 1949, p. 645.

11 Duke-Elder, S.: Text-Book of Ophthalmology, Vol. 3, St. Louis, C. V. Mosby Company, 1941.

12. Odqvist, B.: The Prognosis in Central Vein and Tributary Vein Thrombosis of the Eye Not Treated with Heparin, Acta ophth. **24**:210, 1946.

satisfactory prognosis. After studying 300 cases of occlusive vascular disease of the retina, he reported preservation of useful visual acuity in 16 of 36 cases of thrombosis of the central retinal vein. Brændstrup [4] analyzed a total of 131 cases of occlusion of the central retinal vein. When 62 cases of hemorrhagic glaucoma were excluded, nearly normal vision was obtained in about 20% of the remaining 69 cases. He further concluded that thrombosis of the central vein was an affection with a distinct tendency to spontaneous reparation and that the resultant visual acuity depended largely upon the involvement of the sensitive macular area, the extent of which seems to be governed solely by fate. Jensen [13] observed that the initial and the final visual acuity did not exceed 0.1 in about one-half of a series of 42 patients with tributary-vein thrombosis. In only 1 of the 29 patients did secondary glaucoma develop.

Our control series consisted of 140 untreated patients with complete occlusion of the central retinal vein, or a total of 148 eyes. The average visual acuity for all eyes at the time of the first examination was 0.08. Secondary glaucoma developed or was present at the time of the initial observation in 38 patients.

TABLE 4.—*Course in Untreated Retinal-Vein Thrombosis*

	Central Vein		
	Complete	Incomplete	Tributary Vein
No.	79	11	71
Observation period	3 mo.-20 yr.	1-12 yr.	6 mo.-20 yr.
Visual acuity			
Initial	0.088	0.420	0.319
Final	0.079	0.546	0.388
Vision improved	15%	36%	42%
Vision unchanged	35%	54%	27%
Vision worse	49%	9%	31%
Secondary glaucoma	43%	0	7%
Enucleation	23%	0	6%

Enucleation was necessary in 18 eyes. Follow-up letters were mailed to all the 140 patients, and 79 replies were received, permitting an observation period of from 3 months to 20 years, in which (Table 4) the condition of 49% appeared to have grown worse and secondary glaucoma developed in 43%. In 35% the condition was unchanged; in only 15% had it improved. The final average visual acuity (0.079) was slightly less than that observed at the initial examination (0.088).

Because of the implication [4] in the literature that a much better prognosis accompanies partial venous occlusion, patients with this condition were studied separately. A total of 25 cases, and as many eyes, were reviewed. The average duration of symptoms before the initial examination was approximately 18.7 days. The visual acuity for the 25 patients at the time of the initial examination was 0.311. Follow-up letters were likewise sent to these patients, and an adequate reply was obtained from 11 persons. In the 1- to 12-year observation period (Table 4) only one had become worse, and in none had secondary glaucoma developed. In 54% the condition was unchanged, whereas in 36% it had improved. In this group the final average visual acuity (0.546) was actually somewhat improved over that observed initially (0.420).

13. Jensen, V. A.: Clinical Studies of Tributary Thrombosis in the Central Retinal Vein, Acta ophth., Supp. 10, 1936.

Follow-up observation has been possible in 71 patients with thrombosis of retinal tributary veins. The average visual acuity at the time of the initial examination was 0.319, whereas that at the final examination was 0.388. In the 6-month-to-20-year observation period, the condition of 42% (30) of these patients appeared to have improved; that of 27% (19) was unchanged, while that of 31% (22) had grown worse. Secondary glaucoma had developed in 7% (5); enucleation was required in 6% (4).

METHOD OF STUDY AND TREATMENT

Anticoagulant therapy was carried out on 47 patients with occlusive vascular disease of the retina (Tables 5 and 6) seen in the department of ophthalmology at the University Hospital during the period from May 1941 to April 1951. The material is selective, inasmuch as treatment was largely limited to patients whose circumstances favored prolonged therapy. Administration of the anticoagulants was under the supervision of two members of the department of internal medicine, who made daily observations on the hospitalized patients and assumed responsibility for checking on those receiving outpatient treatment. Thirty-six patients were hospitalized, and

TABLE 5.—*Anticoagulant Therapy in Forty-Seven Cases of Retinal Occlusive Vascular Disease*

Type		Cases
Retinal-vein thrombosis		33
Central retinal vein	26	
Complete	20	
Partial	6	
Retinal tributary vein	7	
Retinal-artery occlusion		7
Central retinal artery, partial	4	
Branch retinal artery	2	
Macular hemorrhage (? embolic)	1	
Diabetic retinopathy		7
Total		47

11 were treated entirely as outpatients. Four received only heparin; 27 received heparin and bishydroxycoumarin U. S. P., and the remainder received only bishydroxycoumarin.

Heparin was administered intravenously by intermittent injections or by continuous infusions; long-acting depository preparations were used in a few patients. The heparin dosage was controlled by frequent determinations of the blood-clotting time (Lee and White). Prolongation of the clotting time to a figure twice the pretreatment value was regarded as satisfactory. When used in conjunction with bishydroxycoumarin, heparinization was continued until bishydroxycoumarin had reduced the prothrombin concentration to the desired therapeutic range, a period averaging about 2.8 days. The manner of bishydroxycoumarin administration has been described in an earlier report.[14] Daily prothrombin determinations were made while the patients were hospitalized. Upon establishment of the maintenance dose of bishydroxycoumarin, the patients were discharged, to be followed at intervals of from 7 to 10 days. The one-stage, unmodified prothrombin test of Quick was employed. Prothrombin activity was expressed in terms of the per cent of normal prothrombin concentration. Twenty to 30% of the normal concentration was the therapeutic goal when bishydroxycoumarin was employed.

Table 7 summarizes the interval between the initial symptom and the beginning of anticoagulant therapy in these patients. The sex and age distribution and the presence or absence of hypertension are also indicated. Bishydroxycoumarin was administered to 22 patients with thrombosis of the central retinal vein for an average of three months. Four who received only heparin were treated for an average of 6.7 days. The observation period averaged 7.8 months.

14. Duff, I. F.: The Effectiveness of Anticoagulant Therapy as Observed in 303 Cases, Angiology **1**:170 (April) 1950.

TABLE 6.—*Results of Anticoagulant Therapy in Forty-Seven Patients with Occlusion Vascular Disease of Retina*

Case No.	Name	Sex and Age	Blood Pressure	Eye	Type of Thrombosis	Duration	Treatment			Visual Acuity		Observation Period	Tension	Status	Final Appearance of Retina
							Heparin	Dicumarol®	Duration	Initial	Final				
Central-Retinal-Vein Thrombosis															
1	J. D.	M 49	135/75	O. S.	Partial	9 days	Yes	Yes	44 days	0.8	1.0	20 mo.	N	Improved	Disc hyperemia progressively less; veins slightly full; no hemorrhage, exudates or sheathing
2	N. R.	M 48	128/68	O. S.	Partial	5 wk.	Yes	Yes	4 mo.	0.2	0.6	4 mo.	N	Improved	Few granular hemorrhages; veins slightly full; minimal gliosis
3	C. W.	M 38	106/62	O. D.	Partial	3 wk.	Yes	Yes	1 wk.	0.2	0.3	None	N	Improved	Typical picture; some hemorrhages absorbing; some new hemorrhages; cystic area in macula
4	W. I.	M 52	Unknown	O. D.	Partial	23 days	No	Yes	78 days	0.95	1.0	6 wk.	N	Improved	Many small granular hemorrhages; occasional petechiae; slight venous fulness
5	G. W.	M 61	Unknown	O. D.	Partial	2 wk.	Yes	No	2 wk.	0.60	1.0	18 mo.	N	Improved	Retina normal; no sheathing
6	O. F.	M 69	Unknown	O. S.	Partial	6 days	Yes	No	4 days	0.06	0.01	None	N	Unchanged	Typical picture
7	J. B.	M	118/76	O. D.	Partial	Unknown	Yes	Yes	51 days	0.05	0.2	7 wk.	N	Improved	Typical picture; some hemorrhages absorbing; extensive hemorrhage in other areas; veins engorged
		74		O. S.	Complete; secondary glaucoma	Unknown	..	..	.....	0.025	0.025	.....	Unchanged	Unchanged	Unchanged
8	M. B.	F 44	136/80	O. D.	Complete	2-3 wk.	No	Yes	10 mo.	0.2	0.95	17 mo.	N	Improved	Normal retina; slight vessel tortuosity in macular area
9	A. R.	F 61	160/82	O. S.	Complete	3 wk.	No	Yes	8 mo.	0.05	0.55	9 mo.	N	Improved	Normal fundus except for slight venous fulness and macular pigmentation
10	E. B.	F 66	120/74	O. D.	Complete	24 hr.	No	Yes	3 mo.	0.55	0.95	3 mo.	N	Improved	Normal fundus except for minimal exudate in macular area
11	G. G.	F 52	118/76	O. S.	Complete	Unknown	Yes	Yes	3 mo.	0.6	1.0	14 mo.	N	Improved	Normal fundus, slight venous fulness
12	E. N.	F 63	128/76	O. S.	Complete	6 wk.	Yes	Yes	3 wk.	0.1	0.2	None	N	Improved	Typical picture; edema less; some hemorrhage absorption
13	M. S.	F 47	110/80	O. S.	Complete	3 wk.	Yes	Yes	6 mo.	0.85	0.95	6 mo.	N	Improved	Normal fundus; slight venous dilatation and sheathing
14	A. M.	F 61	192/108	O. D.	Complete	1 wk.	Yes	Yes	11 days	0.05	0.1	22 mo.	N	Unchanged	Typical picture; marked retinal gliosis in macular area
15	F. T.	M 71	200/90	O. D.	Complete	2 wk.	Yes	Yes	2 mo.	0.05	0.05	2 mo.	N	Unchanged	Full and tortuous veins; partial hemorrhage absorption
16	R. W.	M 74	140/78	O. S.	Complete	1 mo.	No	Yes	7 mo.	0.05	0.05	9 mo.	N	Unchanged	Markedly full and tortuous veins; old hemorrhages; scattered exudates
17	W. M.	M 69	150/75	O. D.	Complete	4 wk.	Yes	Yes	36 days	0.2	0.2	3 mo.	N	Unchanged	Typical picture; fewer hemorrhages and less venous engorgement
18	H. G.	M 71	140/100	O. D.	Complete	5 wk.	No	Yes	1 mo.	0.2	0.2	1 mo.	N	Unchanged	Typical picture; no new hemorrhages
19	A. B.	F 54	160/100	O. D.	Complete	6 days	Yes	Yes	10 days	0.025	0.05	15 mo.	N	Unchanged	Typical picture; hemorrhages clearing

TABLE 6.—*Results of Anticoagulant Therapy in Forty-Seven Patients with Occlusion Vascular Disease of Retina—(Continued)*

Case No.	Name	Sex and Age	Blood Pressure	Eye	Type of Thrombosis	Duration	Treatment			Visual Acuity		Observation Period	Tension	Status	Final Appearance of Retina
							Heparin	Dicumarol®	Duration	Initial	Final				
20	W. B.	M 67	140/90	O. S.	Complete	1 mo.	Yes	No	6 days	0.1	0.1	6½ yr.	N	Unchanged	Typical picture
21	M. B.	F 77	200/100	O. D.	Complete	7 wk.	No	Yes	6 mo.	0.35	0.25	7 mo.	N	Worse	Nearly normal veins; early circinoid-like macular changes; many vitreous opacities; increased lens opacification
22	H. K.	M 41	120/80	O. S.	Complete	14 hr.	Yes	Yes	3 mo.	0.05	0.15	4 mo.	N	Worse	Typical picture; increased hemorrhages and exudates
23	D. D.	M 29	130/90	O. D.	Complete	10 days	No	Yes	2 mo.	0.4	0.2	3 mo.	N	Worse	Typical picture; marked retinal gliosis; extensive hemorrhages and exudates
24	G. D.	M 54	190/94	O. D.	Complete	2 days	Yes	Yes	6 wk.	0.05	0.025	6 wk.	N	Worse	Fundus visualization prevented by vitreous hemorrhage
25	J. K.	M 52	148/84	O. D.	Complete	2 wk.	Yes	No	3 days	0.01	0 (Enucleation)	3 days	Increased	Worse	Hemorrhagic glaucoma
26*	A. L.	M 74	180/100	O. D.	Complete	1 wk.	Yes	Yes	12 days	0.2	0.1	7 mo.	N	Worse	Extensive attenuation and sclerosis of entire arteriolar system; full and tortuous veins; edema and hemorrhages
							Tributary-Vein Thrombosis								
1	O. L.	M 58	122/72	O. D.	Superior temporal	1 wk.	No	Yes	7 mo.	0.05	0.55	6 mo.	N	Improved	Marked retinal improvement; veins normal; macular pigmentation
2	D. S.	F 68	178/82	O. D.	Inferior temporal	2 wk.	No	Yes	3 mo.	0.05	0.6	3 mo.	N	Improved	Definite macular star; minor edema and exudates; persistent hemorrhages
3	E. B.	M 42	135/94	O. S.	Superior temporal	3 wk.	No	Yes	3 mo.	0.55	1.0	5 mo.	N	Improved	Site of previous occlusion unrecognized; vessels normal; gliotic sheen above macula
4	J. S.	M 45	120/86	O. S.	Inferior temporal	1 mo.	Yes	Yes	2½ mo.	0.55	1.0	2½ mo.	N	Improved	Hemorrhages absorbing; exudates present
5	D. C.	M 60	160/90	O. D.	Superior temporal	1 mo.	No	Yes	1 yr.	0.2	0.2	1 yr.	N	Unchanged	Vein empty and white; scattered rosette hemorrhages; macular circinoid-like changes
6	F. R.	F 58	246/130	O. S.	Inferior nasal	Unknown	Yes	Yes	3 mo.	0.55	0.35	1 mo.	N	Worse	Many hemorrhages; disappearance of edema and exudates
7	P. K.	F 59	155/100	O. D.	Inferior temporal	4 mo.	Yes	Yes	9 days	0.2	0.025	5 wk.	N	Worse	Extensive glial retinal scarring; temporal, macular, and foveal circinate changes
							Retinal-Artery Occlusion								
1	B. S.	M 46	120/76	O. D.	Cilio-retinal	2 wk.	Yes	Yes	1 mo.	0.05	0.88	1 mo.	N	Improved	Extensive edema clearing in macula
2	E. S.	F 60	210/120	O. S.	Partial central	4½ hr.	Yes	Yes	5 days	0.01	0.01	5 days	N	Unchanged	Disk margin hazy and edematous; hemorrhages and exudates unchanged; cherry-red spot; some reopening of involved vessels

* Central-artery occlusion of the right eye with chronic noninflammatory glaucoma in each eye.

3	L. D.	F 48	240/160	O. D.	Partial central	Unknown	Yes	Yes	6 days	0.01	0.01	12 days	N	Unchanged	Extensive glial sheathing; spotty exudates; cherry-red spot; fatal cerebrovascular accident
4	I. L.	F 70	180/90	O. D.	Partial central	36 hr.	Yes	Yes	17 days	0.01	0.01	17 days	N	Unchanged	Extensive optic atrophy; attenuation of arterioles
5	E. C.	M 50	180/110	O. S.	Partial central	1 wk.	No	Yes	12 days	0.01	0.0	12 days	N	Worse	Complicating cataract; obliteration of anterior chamber; iridal and corneal vascularization
6	C. C.	M 42	118/82	O. S.	Superior temporal	3 wk.	Yes	Yes	3 mo.	1.0	0.6	27 mo.	N	Worse	Minor arterial attenuation and sheathing; macular gliosis
7	L. C.	F 29	180/80	O. S.	Macular hemorrhage; embolus (?)	6 days	No	Yes	20 days	0.2	1.0	20 days	N	Improved	Macular area normal in all respects
									Diabetic Retinopathy						
1	W. M.	F 32	125/85	O. D. O. S.	O. U.: Severe diabetic retinitis proliferans	6 wk.	No	Yes	6 mo.	0.5 0.45	0.85 0.55	6 mo.	N	Improved O. U.	Clearing macula with few scattered microaneurysms; retinitis proliferans more extensive; new-formed vessels O. U.
2	V. F.	F 37	180/95	O. D. O. S.	O. U.: Early diabetic retinopathy with angiospasm	Unknown	No	Yes	6 wk.	0.45 0.80	1.0 1.0	6 wk.	N	Improved O. U.	O. D.: A few microaneurysms; definitely less hemorrhages O. S.: As in O. D. except for waxy exudates
3	J. S.	M 67	Unknown	O. D. O. S.	O. U.: Diabetic retinopathy	Several mo.	No	Yes	7 mo.	0.4 0.55	0.5 0.6	7 mo.	N	Improved O. U.	Numerous microaneurysms; granular hemorrhages; saccular venous changes; extensive arteriosclerotic changes
4	L. U.	M 51	185/100	O. D. O. S.	O. U.: Diabetic arteriosclerotic hypertensive retinopathy; retinitis proliferans O. S.: Rubeosis irides; secondary glaucoma	3 mo.	No	Yes	6 wk.	0.25 0.05	0.4 0.05	6 wk.	O. U.: N	Improved O. D.: unchanged O. S.	Many waxy exudates and microaneurysms; many superficial hemorrhages O. D.: hemorrhages and exudates clearing O. S.: Unchanged
5	M. M.	F 58	187/73	O. D. O. S.	O. U.: Severe diabetic retinopathy; retinitis proliferans	1 yr.	No	Yes	2 mo.	0.002 0.05	0.05 0.05	2 mo.	N	Unchanged O. U.	O. D.: Unchanged O. S.: Vitreous hemorrhage obscuring retina
6	M. T.	F 41	122/74	O. D. O. S.	O. D.: Diabetic retinopathy; early retinitis proliferans O. S.: Far-advanced retinitis proliferans, vitreous hemorrhage	3 mo.	No	Yes	3 mo.	0.60 0.05	0.6 0.05	3 mo.	N	Unchanged O. U.	O. D.: No change; decreased disk capillarity O. S.: Recent vitreous hemorrhage obscuring disk
7	W. G.	M 43	120/80	O. D. O. S.	O. S.: Retinitis proliferans; rubeosis irides; glaucoma O. S.: Diabetic retinopathy; early retinitis proliferans	6 wk.	No	Yes	6 mo.	0.30 1.00	Nil 1.0	6 mo.	O. D.: Increased O. S.: N	O. D.: Worse O. S.: Unchanged	O. D.: Rubeosis irides with ectropion uveae; marked retinitis proliferans with extensive glaucomatous atrophy O. S.: New-formed vessels; full and saccular veins; numerous microaneurysms; scattered granular hemorrhages

The majority of these patients, except for the presenting complaint and the incidence of essential hypertension, were in reasonably good health. In one patient (Case 26) partial occlusion of the central retinal artery was present, in addition to complete thrombosis of the central retinal vein in the same eye.

Of the group with thrombosis of tributary retinal veins, preliminary heparinization was employed in three. All patients received bishydroxycoumarin, the duration of therapy averaging four months. The observation period averaged 4.5 months. Aside from essential hypertension, the general health of this group was good.

Of the seven patients with occlusive arterial disease of the retina, five received preliminary heparinization. Bishydroxycoumarin was administered for an average of 25 days. The observation period averaged four months. Associated disease states are of interest in this group, in addition to the presenting complaint and the incidence of essential hypertension. Prior to the development of retinal-artery occlusion, two patients (Cases 3 and 5) had experienced cerebral vascular accidents, in one of whom (Case 3) a second, and fatal, cerebral hemorrhage occurred during anticoagulant therapy.

All seven patients presenting diabetic retinopathy received bishydroxycoumarin without previous heparinization. The average period of treatment, as well as the average extent of

TABLE 7.—*Interval Between Initial Symptoms and Beginning of Anticoagulant Therapy*

Type	Sex		Age, Yr.			Average		No. with Normal Blood Pressure	No. with Essential Hypertension*	Blood Pressure Unknown	Symptom Time†	
	Male	Female	Average	Lowest	Highest	Systolic	Diastolic				Average, Days,	Unknown
Thrombosis												
Central retinal vein (26 cases)												
Partial	7	..	56.1	38	74	121	70	4	0	3	18	1
Complete	10	9	59.3	29	77	152	87	10	9	0	19	1
Total	17	9	58.4	..	..	146	84	14	9	3	19	2
Retinal tributary vein (7 cases)	4	3	55.7	42	68	159	94	2	5	0	20	1
Retinal arteries (7 cases)	3	4	48.5	29	70	108	102	3	4	0	8.4	1
Diabetic retinopathy (7 cases)	3	4	47.0	32	67	153	84	3	3	1	72-360	2

* Blood pressure in excess of 150/90.
† Time between initial symptoms and beginning of anticoagulant therapy.

observation, was four months. Associated disease states in this group included essential hypertension and, in one case, peripheral vascular disease. The diabetes was under satisfactory control in all patients.

CLINICAL OBSERVATIONS

Tables 8 and 9 summarize the final visual status of the patients for whom anticoagulant therapy was employed. Sixteen of 33 patients (48%) with retinal-vein thrombosis appear to have improved. Their initial visual acuity averaged 0.39; at the final examination it was 0.76. The condition of nine patients (27%) was unchanged, and that of eight (24%) had grown worse. Hemorrhagic glaucoma necessitated enucleation of one eye.

The condition of 12 (46%) of 26 patients with thrombosis of the central retinal vein improved; that of 8 (30%) remained unchanged, and that of 6 (23%) grew worse. The average visual acuity for the group was 0.30 initially and 0.40 at the final observation; the difference, 0.10, is not impressive. For those patients who showed improvement, however, the respective values for visual acuity were 0.43 and 0.72; the difference, 0.29, is somewhat more significant. The material is more satisfactorily analyzed by the approach utilized by Ploman.[17] He divided his patients into four groups according to the last recorded acuity of vision (Group A had

1.0 to 0.9; Group B, 0.8 to 0.4; Group C, 0.3 to 1/60, and Group D, 0.5/60 to 0). The first group recovered practically without ill effects; in the second, sight was regained sufficiently for reading purposes; the third group of patients could see to

TABLE 8.—*Visual Acuity in Cases of Retinal Occlusive Vascular Disease Treated with Anticoagulants (University of Michigan)*

	No. of Cases	Vision Improved*	Average Visual Acuity		Observation Period	Vision Unchanged	Vision Worse	Glaucoma	Enucleation
			Initial	Final					
Retinal-vein thrombosis									
Central vein	26	12 (46%)	0.43	0.72	7.8 mo.	8 (30%)	6 (23%)	1	1
Tributary vein	7	4	0.30	0.86	4.5 mo.	1	2	0	0
Total	33	16 (48%)	0.39	0.76	.....	9 (27%)	8 (24%)	1	1
Retinal-artery occlusion									
Central artery	4	0	....	....	11 days	3	1	0	0
Branch artery	2	1	0.05	0.36	14 mo.	0	1	0	0
Macular hemorrhage	1	1	0.20	1.00	20 days	0	0	0	0
Total	7	2 (29%)	....	....	.....	3	2	0	0
Diabetic retinopathy (7 patients)	14 eyes	7 eyes	0.48	0.70	.....	6 eyes	1 eye	1	0

* Demonstrating an increase of at least 0.1 in visual acuity.

TABLE 9.—*Result of Anticoagulant Therapy (Classified After Ploman) in Cases of Thrombosis of Central Retinal Vein*

Group	No. of Cases	Average Age	Before Treatment		Treatment Duration, Days	Observation Period	After Treatment		Fundus
			Symptom Time	Average Vision			Average Vision	Tension	
A	7	53.2	(unknown in 1) 14.6 days	0.65	114	11 mo.	1.0-0.9	Normal	Normal in 6 cases except for slight venous fulness (4), slight venous sheathing (1), and tortuosity in macula (1); persistent macular exudates (1); granular and petechial hemorrhages persisted in 7th case
B	2	54.5	28 days	0.125	180	6½ mo.	0.8-0.4	Normal	Normal in 1 case except for macular pigmentation; in 2d case few granular hemorrhages and minimal gliosis and fulness of veins
C	16	61.6	10.2 days (unknown in 1)	0.191	54	None in 2; 6½ yr. in 1; 6.7 mo. in 13	0.3-1/60	Normal	Persistent hemorrhages in 15 cases; some hemorrhage absorption in 6; increased or new hemorrhages in 2; tortuous and engorged veins in 3; improvement in veins in 2; vitreous hemorrhage in 1; macular changes in 4; vitreous opacities and lens opacification in 1
D	1	52.0	15 days	0.01	3	3 days	0.5/60-0	Increased	Hemorrhagic glaucoma; enucleation required
Total	26	58.4	18.6	0.302	78	7.8 mo.	0.40	.....	

walk, and the remainder were practically blind. On this basis, 27% (7) of our patients (Table 9) fall in Group A; 7%, in Group B; 62% (16), in Group C, and 4% (1), in Group D. The funduscopic details were essentially normal at the final examination in seven of the nine patients in Groups A and B. For five of these patients the original diagnosis was complete thrombosis of the central retinal vein. Retinal abnormalities were persistent, and sometimes prominent, in the remaining 19 patients. New retinal hemorrhages had occurred in two patients; in a third a vitreous hemorrhage had developed.

The number of cases of tributary-vein thrombosis is too small for detailed analysis. Four of the seven patients showed improvement, with an increase in average visual acuity from 0.30 before treatment to 0.86 at the last examination. The condition of one patient was unchanged; that of two grew worse, and in none did glaucoma develop. Of the two cases in Ploman's Group A, the fundus of one became essentially normal, while persistent exudates and absorbing hemorrhages were observed in the second. Marked improvement in the fundus occurred in a third patient, whose visual acuity, however, did not return to normal. The remaining four patients exhibited varying degrees of persistent exudates, hemorrhages, and macular changes.

Of the seven patients with lesions of retinal arteries, only two (29%) improved. One of these (Case 7), with a macular hemorrhage, possibly on an embolic basis, of six days' duration, had regained normal vision and a normal fundus at the end of 20 days of treatment. The second (Case 1), with occlusion of a cilioretinal artery of two weeks' duration, had improved considerably both with regard to visual acuity and the appearance of the retina after one month of treatment. The fundus of a third patient (Case 6), with occlusion of the superior temporal artery of three-weeks' duration, had improved when treatment was discontinued. Twenty-seven months later, however, the visual acuity was found to have dropped from 1.0 to 0.6; the fundus revealed minor arterial attenuation, sheathing, and macular gliosis. At the last observation on the remaining four patients, all of whom had sustained a partial occlusion of the central retinal artery, the condition of three remained unchanged, and one had become blind.

Of the 14 eyes with diabetic retinopathy, 7 demonstrated improvement in visual acuity. The average visual acuity prior to treatment was 0.48; the average acuity at the last observation was 0.70. In six eyes visual acuity remained unchanged, while in one hemorrhagic glaucoma developed and the eye became amaurotic. The fundi in one patient (Case 1) showed considerable improvement, with absorption of the hemorrhage in the macular area; neovascularization, however, was present in both eyes. The fundi of three other eyes showed variable hemorrhage absorption. Funduscopic details remained unchanged in six eyes. Vitreous hemorrhages, occurring in two eyes, obscured visualization of the fundi. As noted above, glaucoma developed in the remaining eye.

HEMORRHAGIC COMPLICATIONS

Bishydroxycoumarin induced bleeding in 13 (28%) of the 47 patients. Bleeding was sufficiently severe to terminate the therapy of seven patients (15%); it was the cause of rehospitalization of one patient, and there was one associated death. Minor ecchymoses were common; hematoma developed in two patients; hemarthrosis occurred in three men, and five patients experienced gross hematuria. Epistaxis occurred in two patients, and severe hypermenorrhea was observed in another patient. Large and repeated doses of vitamin K (menadione bisulfite) appear beneficial in reversing the hypoprothrombinemia and terminating the associated bleeding. Hemorrhage from heparin did not occur. A lower incidence of hemorrhagic complications has been reported by Rosengren,[1d] Palomar,[10] MacLean and Brambel,[1b] Banks-Smith,[1c] and Rosenthal and Guzek.[1a] Huggett and Juler [11] emphasized the danger of heparin in association with the treatment of occlusive vascular

disease of the retina. They noted an increase in the retinal hemorrhage of the affected eye in five of their nine cases of thrombosis of the central vein. Small retinal hemorrhages were observed in one unaffected eye, and bleeding developed at other sites. In the series described by us, increased retinal hemorrhages were sometimes seen in the affected eye. In addition, vitreous hemorrhages occurred in three patients. We cannot be certain, however, that anticoagulant therapy can be held responsible for the bleeding tendency in these cases, in view of the prominence of hemorrhage in the natural course of occlusive vascular disease of the retina.

Sudden death may be associated with occlusive arterial disease of the retina.[14,7] An accident of this type in our material[15] (Case 3) is of interest. The patient, a woman aged 43, with essential hypertension, was hospitalized for evaluation of her cardiovascular status. During the course of the studies occlusion of the central retinal artery developed. Anticoagulant therapy consisted in use of heparin and bishydroxycoumarin. The prothrombin level was satisfactorily maintained at between 20 and 30% of normal concentration until the 13th day of treatment, when it suddenly dropped to 5% of normal. At this time the patient lapsed into coma and presented signs of left hemiplegia and meningeal irritation. Despite intravenous injection of vitamin K, death occurred in approximately four hours. Permission for necropsy could not be obtained. A cerebral hemorrhage is assumed to have been the cause of death. The association of this accident with the excessive hypoprothrombinemia may well have been more than coincidental.

COMMENT

Ploman[12] outlined the indications for anticoagulant therapy in retinal-vein thrombosis. Above all, the physician must be equipped to handle this form of therapy. Lack of satisfactory laboratory control of bishydroxycoumarin dosage constitutes an absolute contraindication. Ploman observed that the best results of treatment were obtained in the younger patients and those in whom the process is less severe and of brief duration. In our experience, duration of symptoms is not necessarily related to prognosis. The magnitude of loss of visual acuity, moreover, should not be used as an absolute guide to selection of patients. Age and the presence or absence of hypertension do not appear to be particularly significant with regard to the likelihood of restoration of sight. There appears to be no reason to treat the patient with extensive degenerative macular changes or the patient in whom secondary glaucoma has developed. Otherwise, if the patient still has fair vision, anticoagulant therapy may be worth considering. It is our custom to continue treatment until visual acuity shows no further improvement or until the appearance of the retina has become stationary. The collected experience, however, does not definitely establish the superiority of long-term anticoagulant therapy over a short, intensive period of treatment with heparin. There can be no doubt that long-term bishydroxycoumarin administration exacts a price in terms of hemorrhagic complications.[16] In our experience, significant bleeding occurred in 28% of the patients and caused termination of treatment in 15%. Bleeding required

15. Duff, I. F., and Shull, W. H.: Fatal Hemorrhage in Dicumarol Poisoning with Report of Necropsy, J. A. M. A. **139**:762 (March 19) 1949.

16. Nichol, E. S.: The Risk of Hemorrhage in Anticoagulant Therapy, Ann. West. Med. & Surg. **4**:71 (Feb.) 1950.

rehospitalization in one instance, and one unfortunate fatality occurred during treatment.

Anticoagulant therapy has been employed in the treatment of occlusive vascular disease of the retina since 1937.[1a-d] On the basis of the experience with this form of therapy reported in the world literature and of that gained in this study, the following impressions have emerged: After thrombosis of the central retinal vein (158 cases) 58% of the patients may be expected to demonstrate an improvement of at least 0.1 in visual acuity (Table 10). A final visual acuity in the range of 0.6 to 0.76 may be achieved in about 58%; approximately 28% may be expected to regain normal vision. The visual acuity in about 19% remains unchanged; that of 23% grows worse, and 9% of patients may be expected to have glaucoma. After thrombosis of a tributary vein (102 cases) approximately 61% may be expected

TABLE 10.—*Prognosis of Retinal-Vein Thrombosis When Treated with Anticoagulants*

Type	Source	Cases	Vision Improved*	Vision Unchanged	Vision Worse	Glaucoma	Enucleation
Central retinal vein	Collected	132	80 (61%)	22 (17%)	30 (23%)	13 (10%)	7 (5%)
	Univ. Mich.	26	12 (46%)	8 (31%)	5 (23%)	1 (4%)	1 (4%)
Total		158	92 (58%)	30 (19%)	36 (23%)	14 (9%)	8 (5%)
Tributary retinal vein	Collected	95	58 (61%)	20 (21%)	17 (18%)	2 (2%)	1 (1%)
	Univ. Mich.	7	4 (57%)	1 (14%)	2 (29%)	0	0
Total		102	62 (61%)	21 (20%)	19 (19%)	2 (2%)	1 (1%)

Type	Source	Cases	How Treated	Vision Improved*	Average Initial Visual Acuity	Final Visual Acuity
Central retinal vein	Collected	81	Heparin	48 (59%)	0.25	0.60
		12	Dicumarol®	10 (83%)	0.23	0.70
	Univ. Mich.	26	Heparin and Dicumarol®	12 (46%)	0.43	0.72
Total		119		70 (59%)		
Tributary retinal vein	Collected	77	Heparin	44 (57%)	0.33	0.68
		9	Dicumarol®	6 (67%)	0.18	0.68
	Univ. Mich.	7	Heparin and Dicumarol®	4 (57%)	0.30	0.56
Total		93		54 (58%)		

* Demonstrating an increase of at least 0.1 in visual acuity at last observation.

to improve, a final visual acuity in the range of 0.60 to 0.86 may be achieved in approximately 58%, and 29% may be expected to regain normal vision. In 20% of cases vision remains unchanged; that of 19% grows worse, and 2% have glaucoma. It is quite plain that, despite anticoagulant therapy, persistent and significant abnormalities of the retina are common.

Anticoagulant therapy has been disappointing in cases of occlusive arterial disease of the retina, a fact anticipated when one recalls that the retina may suffer irreparable damage within 20 minutes after an arterial occlusion. This fact[11] is a handicap to the effective institution of treatment. That two of our patients with retinal-artery lesions did improve and that similar cases have been reported[17] in the literature justifies the use of anticoagulants if the circumstances are favorable.

In three of four cases of diabetic retinopathy in which MacLean and Brambel[1b] administered bishydroxycoumarin and rutin, improvement of visual acuity and absorption of hemorrhages were described. In our experience, 7 of 14 eyes with

17. Rychener.[11] Qvist.[1q] Blum and Jeanneret.[1a] Arkle.[5a] Girault-Dangely.[5b]

diabetic retinopathy have demonstrated some improvement in visual acuity. The fundus of one patient showed significant improvement. Absorption of retinal hemorrhages was evident in three other eyes. More experience is required, however, before any definite statement can be made with regard to the benefits of anticoagulant therapy in this group of patients. There is no substantial evidence in our limited observation that anticoagulant therapy prevents neovascularization (retinitis proliferans); in fact, in two eyes there was a definite progression in the extent of new-vessel formation.

SUMMARY

The prognosis for adequate visual acuity following untreated thrombosis of a tributary or central retinal vein is discouraging. In a control series of 79 untreated patients with complete occlusion of a central retinal vein, the condition of 49 grew worse, and secondary glaucoma developed in 43%. Only 15% of these patients showed improvement, whereas the condition of 35% remained unchanged. The prognosis appears to be much less grave for untreated incomplete thrombosis of a central retinal vein.

The collected experience with anticoagulant therapy after thrombosis of a tributary or central retinal vein indicates that in 58% the prognosis for visual improvement is favorably influenced; the frequency, moreover, of secondary glaucoma appears to have been encouragingly lowered. Under treatment, however, not all will recover: The visual acuity of 19% will remain unchanged, and that of 9% will definitely grow worse. A short term of intensive treatment with heparin appears to produce results as favorable as those obtained with prolonged use of bishydroxycoumarin (dicumarol®). The incidence of hemorrhage in long-term treatment with bishydroxycoumarin, moreover, is appreciable. This is the basis for recommending heparin for general use. Institution of treatment must be prompt after thrombosis or occlusion of a retinal artery if the results are to be favorable. More experience is required before anticoagulant therapy can be recommended for treatment of other types of retinal occlusive vascular disease.

ABSTRACT OF DISCUSSION

DR. A. E. MACDONALD, Toronto, Canada: May I thank Dr. Falls for the privilege of studying his paper in advance? It is an excellent report, with a good control series, and, deals with a surprisingly large number of cases observed over a period of 10 years.

In 1938 Dr. Charles Best asked me about my results in the treatment of retinal vascular occlusion. He had just returned from Sweden, where he found great interest in the purification of heparin. After our discussion, it occurred to me that the rich blood supply of the choroid made an ideal medium for the use of this drug, and in 1940 I reported three cases of occlusion with heparin treatment. Since then I have treated all occlusions as early as possible, regardless of the duration of loss of vision or the extent of involvement.

Heparin has been given intravenously, with administration of dicumarol® by mouth, at the beginning of bed rest. These drugs are used extensively at the Toronto General Hospital, especially by Dr. Gordon Murray, who long ago treated his 2,000th patient, without a fatality. I am grateful to Dr. Murray and his staff, who supervise the determinations of clotting and prothrombin times and adjust the dosage with great care. The dangers are obvious, but the risk is accepted by the patient after adequate explanation.

Our series at Toronto is less imposing than Dr. Falls's but possibly somewhat more encouraging, as two patients with complete occlusion and two with branch-

artery occlusion regained normal vision. Besides these four, a patient with aphakia had, after treatment, vision of 6/60 + 1 in the only remaining eye; while he was not able to read, he was happy with guiding vision. Another gained a visual acuity of 6/18 — 1 from 6/60 + 1. Three maintained their pretreatment sight. The 10th patient has steadily lost ground, vision having decreased from 6/24 to counting fingers at 1 meter, and now, after one year, hemorrhages are numerous and the macular region is badly disorganized. In none of the group has the eye been lost or become glaucomatous.

Dr. Falls has chosen improvement in vision of 0.1 as a criterion of success. I would suggest that even the retention of the eye and a full peripheral field be considered a satisfactory result. It seems that the hard way is the best way. The complications of the treatment are manifold, and the ophthalmologist is glad to share the responsibility and to avail himself of the teamwork of a well-organized group of internists. New drugs are appearing, and it is hoped that phenylindandione ("danilone") and BL5 (Abbott) will reduce the dangers. I have twice had the prothrombin time go over 50 seconds with dicumarol® therapy. One patient suffered no ill effect; the other had the appearance of hematuria, and treatment was stopped. When he returned to Toronto one year later his vision had improved to 6/6 — 2. I am satisfied to report that of 10 cases, the results were excellent in 4, good in 2, fair in 3, and poor in 1.

Our results of anticoagulant treatment are summarized in the following tabulation:

Patient	Age	Retina	Vision		Comment
			Pre-treatment	Post-Treatment	
Mrs. M.	70	Complete	F 2 m.*	4/36	1940 report
Mrs. R.	48	Tributary	6/60+1	6/18-1	1940 report; twig; at first whole lower retina and macula
Mrs. O.	48	One-half	6/60+1	6/6-1	1940 report; twig occluded; at first whole lower retina and macula
Mrs. W.	57	Tributary	6/18	6/9+3	Blood pressure: 216/120
Mrs. W.	58	Tributary	6/6-2	6/6-1	Died Dec. 1947, probably of pulmonary thrombosis
Mr. O'C.	82	Complete	F 2 m.	6/60+1	Aphakia; full field
Mrs. S.	70	Tributary	F 3 m.	F 3 m.	Macular degeneration; full field
Mr. B.	35	Complete	6/60 part	6/6-2	Early treatment within 30 hr.
Dr. R.	73	Complete	F 4 m.	F 4 m.	Late case—vague report of 6/36 (f) vision
Mrs. R.	41	Complete	6/24	F 1 m.	Slowly becoming worse

* F indicates vision limited to counting fingers.

DR. IRVING H. LEOPOLD, Philadelphia: Since the advent of anticoagulants in the therapy of occlusive vascular disease, both bishydroxycoumarin (dicumarol®) and heparin have been used by ophthalmologists in treatment of this condition. It is fully realized that these agents have no power to dissolve thrombi already present, but they may be helpful in preventing the extension of an existing thrombus and the formation of thrombi initially.

The chief complication of this form of therapy is spontaneous bleeding. The antidotes for heparin are basic substances, such as protamine, toluidine blue, and, for bishydroxycoumarin, vitamin K_1, 50 to 100 mg. by injection every 2 to 24 hours. Blood transfusions are valuable for overdoses of both heparin and bishydroxycoumarin.

These facts are well known, but as ophthalmologists we are concerned with many other problems, and it is these that Drs. Duff, Falls, and Linman have attempted to answer. They have analyzed the cases in the literature and their own cases at the University of Michigan and have thereby massed a considerable body of data, which they have analyzed carefully. It is their conclusion that eyes with venous occlusion which are treated with anticoagulants do slightly better than those not so treated. They have shown that the time at which the patient presents himself for therapy after the onset of the occlusion is not an important factor in the final visual result. Some eyes which were not treated for several weeks after onset of

occlusion had a favorable end-result, whereas others which were treated within the first 24 hours did very poorly. The reduction in incidence of secondary glaucoma after anticoagulant therapy is significant. Perhaps Dr. Falls may have an explanation for this effect.

The authors' statistics failed to show any significant benefit from prolonged therapy. This is important, for, as Falls and his co-workers have noted, complications occur with heparin and dicumarol® therapy. Complications are much more frequent with dicumarol® therapy. It is this drug which is used over a long period because of its ease of administration. If the results with short-term and with long-term therapy are equally good, the bleeding complications of anticoagulant treatment would be reduced; i. e., more patients would be treated with heparin rather than bishydroxycoumarin; patients would then be hospitalized, where they could be more closely watched, and fewer undesirable effects would be encountered.

Anyone planning to use anticoagulants must have an adequate knowledge of the contraindications, such as hypoprothrombinemia, which may occur with hepatic disease, and deficiencies in vitamins K and C. Blood dyscrasias and renal insufficiencies also should prevent the use of anticoagulants. One should know the effect of other agents on the prothrombin levels. Salicylates may lower the prothrombin content, and corticotropin (ACTH) and cortisone may increase the tendency to thrombosis. Ophthalmologists using this form of therapy should, of course, be interested in new anticoagulants, such as paritol® (a polysulfuric acid ester of polyanhydromannuronic acid) and tromexan® (ethyl bis-[4-hydroxy-2-keto-3-a-benzopyramyl] acetate).

Although these studies show some beneficial effects of anticoagulants, it is obvious that almost 50% of eyes with retinal venous occlusion will not improve even with this form of therapy. If the effectiveness of anticoagulant therapy is to be increased, some method of using it prophylactically must be found. Unfortunately, the majority of patients about to suffer retinal-vein occlusion have no warning signs, and the onset of the disease is sudden.

This study has been thorough, timely, and extremely helpful in defining the present position of anticoagulants in ocular vascular disease.

Dr. Harold F. Falls, Ann Arbor, Mich.: I wish to thank the discussants for their contributions, which further elaborated details not covered in the presentation of the paper.

You asked specifically one question: Do I have any explanation for the reduction in incidence of secondary glaucoma in the treated patients? We perused our material thoroughly, hoping to explain this lowered occurrence of secondary glaucoma. There are two possible explanations: (1) the high degree of selectivity of our material (we chose patients we thought we could help) and (2) the possibility of anatomical vascular anastomoses between the retinal vasculature and the choroidal and/or the vaginal systems. It is conceivable that anticoagulant therapy may augment such anastomoses until sufficient collateral is established to permit normal or near-normal function. One thing is certain, we need to know more about the circulation in and about the optic nerve. More thorough knowledge might explain some of the cases of "partial central-vein occlusion" in which normal vision is recovered.

My associates and I feel that if we had an occlusion of the central retinal vein, we should prefer to have anticoagulant therapy.

THE COMPENSATION MAXIMUM

A New Glaucoma Sign in Aqueous Veins

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ALMOST exactly 10 years ago, Ascher [1] observed an aqueous vein for the first time, laying the cornerstone for his well-known work on the visible elimination of aqueous humor in episcleral and conjunctival veins. Numerous authors have subsequently studied the significance of this visible fluid elimination and its abnormalities.

Ascher,[1] Goldmann,[2] and de Vries [3] described an increase of the clear fluid stream in epibulbar vessels occurring during external compression of the eyeball. This is most obvious in the widening of the clear stratum in stratified recipient vessels. Usually only a few, 2 to 4, of the 20 to 30 outlets of Schlemm's canal carry aqueous humor as far as the surface of the eyeball; each of the outlets, however, may be considered the potential origin of an aqueous vein. In the normal eye, a few of these pathways are favored, owing to anatomical, and probably to small local pressure, differences—the aqueous humor leaves the canal where resistance is lowest. During the compression of the eyeball, however, formerly invisible aqueous veins appear because of the artificially increased hydrostatic potential between Schlemm's canal and the intrascleral veins. Thus, Duke-Elder [4] is justified in calling Schlemm's canal and its outlets a safety valve. The spontaneous aqueous drainage in glaucomatous eyes differs from that in eyes with normal pressure when subjected to artificial increase in pressure. In glaucomatous eyes, also, there is a higher pressure in the anterior chamber, whereas the pressure inside the episcleral veins remains normal or is only slightly increased. In spite of the increase in the hydrostatic potential in the aqueous drainage of glaucomatous eyes, the fluid elimination in their aqueous veins shows no evidence of increase; in some cases of wide-angle glaucoma, Ascher's veins are not to be found at all. Goldmann [5] believed that in eyes with simple

From the Second University Eye Clinic, Vienna, Prof. K. Lindner, Director.

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1. Ascher, K. W.: Aqueous Veins: Preliminary Note, Am. J. Ophth. **25**:31, 1942.

2. Goldmann, H.: Studien über den Abflussdruck des Kammerwassers beim Menschen, Ophthalmologica **114**:81, 1947.

3. de Vries, S.: De zichtbare afoer van het kamerwater, Thesis, Amsterdam, 1947.

4. Duke-Elder, W. S.: The Ocular Circulation, Brit. J. Ophth. **10**:513, 1926.

5. Goldmann, H.: Der Druck im Schlemmschen Kanal bei Normalen und bei Glaukoma simplex, Experientia **6**:110, 1950.

glaucoma an increased resistance of the pectinate ligament interfered with transfer of the aqueous humor, whereas Ascher[6] blamed a narrowing of the intrascleral outlets for the increase in pressure. The statement that a rise in intraocular pressure in simple glaucoma may be due to increased resistance to the aqueous flow is common to the two aspects expressed.

THE BACKFLOW PHENOMENON

I observed the following phenomenon: If a glaucomatous eye was compressed by a finger or, in order that the measurement might be made more exactly, by means of an ophthalmodynamometer (Bailliart), and if the aqueous veins were observed far from the locus of the exerted pressure, an initial increase of clear fluid in the stratified recipient vessels was noticed, such as occurs in eyes with normal pressure as well; if, however, the external pressure was increased, the aqueous stream in many of these aqueous veins slowed down and finally reversed. This slowing occurred when a certain amount of pressure was exerted, and on repetition of this experiment (during the same observation period) practically identical values were required in order to force the venous blood in a direction opposite its normal stream. Blood will first enter the recipient vessel and then the aqueous vein proper; occasionally it will go as far as the origin of the aqueous vein in a scleral emissary. At the present time, more than 400 normal eyes have been observed, a great majority (92%) of which did not present the backflow phenomenon described, even during compression of 150 gm.; glaucomatous eyes, or eyes susceptible to interference with elimination of intraocular fluid and later pressure increase (more than 300 eyes), however, not infrequently showed this backflow phenomenon during a compression of less than 100 gm.

Having observed this difference in response of glaucomatous and of normal eyes to external pressure and its effect on Ascher's veins, I studied the backflow phenomenon on a great number of glaucomatous eyes. Considering that it is often difficult to find the original aqueous vein and its emissary, I restricted my observations to ascertaining the moment of reversal of current in the recipient vessels. I proposed the term "compensation maximum" for that amount of external pressure which is necessary to reverse the current in recipient vessels. My method and the results are extensively discussed in a paper published by Kleinert and Grün.[7]

At the same time that one aqueous vein shows the reversal of current due to external compression, other aqueous veins of the same eye will usually show the same phenomenon; in exceptional instances, single aqueous veins of the same eye showed differences in compensation maximum of more than 15 gm. During the compression, aqueous humor may enter a collateral detour without being subjected to stoppage, thereby causing reading errors. When the dynamometer pressure is released, aqueous humor reassumes its normal current, either immediately or after a short period of turbulence, i. e., mingling of blood and aqueous humor. These phenomena are related to the duration of the pressure and to the amount of aqueous

6. Ascher, K. W.: Backflow Phenomenon in Aqueous Veins of Normal and of Glaucomatous Eyes, Am. J. Ophth. **27**:1074, 1944.

7. Kleinert, H., and Grün, P.: Das Kompensationsmaximum, ein Glaukomsymptom, Klin. Monatsbl. Augenh. **118**:449, 1951.

humor expressed during compression. During this period, the volume of the anterior chamber is somewhat reduced; the intraocular pressure is greatly lowered, and the hydrostatic potential is not high enough to maintain the visible fluid elimination in Ascher's veins. During this hypotony, Schlemm's canal contains blood, as proved gonioscopically; as long as the compression is being exerted, blood is never seen inside Schlemm's canal, despite the fact that in cases with low compensation-maximum readings blood is seen streaming toward the scleral emissaries.

In this connection, it should be mentioned that I, watching simultaneously the origins of the aqueous veins biomicroscopically and the corresponding sections of Schlemm's canal gonioscopically, observed how the blood entered Schlemm's canal during compression of the jugular veins: I stated that the blood did not enter from the epibulbar veins and concluded that it must derive from the intrascleral plexus or from the ciliary veins. When, however, blood leaves the canal of Schlemm after cessation of compression of the jugular vein, it does so through Ascher's veins.

From Kleinert and Grün's observations on the compensation maximum, the conclusion was drawn that there is a relation between dynamometer readings and possible interference with aqueous-humor elimination: If the dynamometer reading is below 100 gm., an obstacle to the outflow of aqueous humor is most probable. In many cases the compensation maximum rose to normal values from its originally low level after successful surgical or medicamentous treatment of the increased ocular pressure; I assumed that in these eyes surgical measures or drugs had either relieved or removed the impediment to aqueous-humor outflow. At present, too little is known about the relations of interference with elimination of aqueous humor to increase in intraocular pressure.

Thomassen [8] found the pressure in epibulbar veins higher during the periods of increase in intraocular pressure, and the pressure readings in these veins became lower before the diurnal decrease of intraocular pressure could be registered; from these observations, Thomassen concluded that changes in intraocular pressure are preceded by corresponding precursory changes in the pressure of the epibulbar veins. This opinion was corroborated by our findings on the compensation maximum in eyes with, or suspected of having, simple glaucoma. It is possible that those eyes with simple glaucoma which showed normal compensation-maximum readings (40%) had normal outflow of aqueous humor at this particular time; some of these eyes, on repetition of the compensation-maximum test, gave pathologically low readings.

In a similar sense, the normalization of compensation-maximum readings after instillation of pilocarpine, physostigmine, or di-isopropyl fluorophosphate (mintakol®) parallels the observations published by Ascher [9] and by Gartner,[10] both of whom noted an increase of the aqueous stream in recipient vessels after instillation of miotics. Alterations in the outlets of Schlemm's canal or in Ascher's veins will

8. Thomassen, T. L.: Experimental Investigations in the Conditions of Tension in Normal Eyes and in Simple Glaucoma, Acta ophth., Supp. 27, p. 1, 1946.

9. Ascher, K. W.: Local Pharmacologic Effects on Aqueous Veins, Am. J. Ophth. **25**:1301, 1942.

10. Gartner, S.: Blood Vessels of the Conjunctiva: Studies with High Speed Macrophotography, Arch. Ophth. **32**:464 (Dec.) 1944.

affect only that part of the aqueous-humor elimination which, following hydrostatic laws, passes through the canal of Schlemm. This part, according to Kinsey,[11] comprises as little as 5% of the whole intraocular-fluid exchange, the remaining 95% being taken care of by osmotic powers. Recently Poos[12] claimed that the fluid exchange of the glaucomatous eye takes place at a higher pressure level, while production and elimination of aqueous humor were practically equal to normal values.

COMPENSATION-MAXIMUM READINGS IN DIFFERENT TYPES OF GLAUCOMA

1. *Simple Glaucoma, Wide-Angle Glaucoma.*—More than 200 eyes were examined; in about 60% the compensation maximum was below 100 gm., irrespective of whether intraocular pressure was permanently or intermittently high. The readings were between 10 and 100 gm.; no definite relation between compensation-maximum readings and the intraocular pressure or the severity of the glaucomatous process was found.

2. *Inflammatory Acute and Chronic Glaucoma.*—During the acute attack aqueous veins were usually invisible; therefore, it was impossible to perform the compensation-maximum test. In the interval between attacks these eyes showed normal compensation-maximum readings. When the readings were pathologic, visual-field defects or early cupping of the disk was found, indicating that the disease in these eyes represented a transition form to simple glaucoma.

These observations might well support the assumption that the glaucomatous attack is not due to primary chronic interference with aqueous-humor elimination, but that the occurrence of such an impediment initiates the transition of acute glaucoma into the chronic type.

3. *Glaucoma with Inflammatory Changes in the Anterior Segment, Secondary Glaucoma.*—The compensation maximum is pathologically low (below 100 gm.) in all eyes still subject to permanent or recurrent pressure increases. After normalization of intraocular pressure and recovery from the causative inflammation, the readings rise to normal values, showing no reflux of blood into aqueous veins during compression of the eyeball by pressures up to 150 gm. Higher pressures were not applied; they are painful, in spite of production of anesthesia with tetracaine or larocaine® (3-diethylamino-2,2-dimethylaminobenzoate).

4. *Suspected Glaucoma.*—In cases of suspected glaucoma determination of the compensation maximum seems to be of practical value. When during the first examination normal Schiøtz readings were found while a low compensation maximum of less than 100 gm. pointed to an obstacle to elimination of intraocular fluid, these eyes later, studied over 24-hour periods, almost always showed increases in intraocular pressure of short duration. On the other hand, clinically suspected eyes with normal compensation-maximum readings produced normal pressure graphs during the following days.

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11. Kinsey, V. E.: A Unified Concept of Aqueous Humor Dynamics and the Maintenance of Intraocular Pressure: An Elaboration of the Secretion-Diffusion Theory, Arch. Ophth. **44**:215 (Aug.) 1950.

12. Poos, F.: Die kausale Genese des genuinen (primären) Glaukoms, von Graefes Arch. Ophth. **151**:71, 1950.

EXPLANATIONS OF THE COMPENSATION-MAXIMUM PHENOMENON

1. Lindner[13] assumed that during compression of the eyeball more than the usual amount of aqueous humor is expressed and leaves the inner eye through deep, invisible veins, and that this increased outflow produces a suction-like, evacuating effect on the visible superficial aqueous veins, followed by influx of blood into the latter. If, however, the superficially located pathways are sufficient for the forcibly increased outflow, the increase of flow in the deep veins will not occur; no suction will be exerted on the superficially located aqueous veins, and no backflow of blood will be observed. In glaucomatous eyes, after surgical improvement of the fluid elimination, which was previously interfered with, probably by anatomical changes in the eliminating veins, no backflow will occur during compression of the eyeball. This assumption by Lindner is in agreement with the normalization of the compensation-maximum readings in eyes subjected to iridencleisis or to trephination for relief of simple glaucoma. During compression of these eyes entrance of fluid (aqueous humor) into the conjunctival filtration bleb can be observed.

Weekers and Prijot[14] observed that after electrocoagulation of all visible arteries and veins of the rabbit eye, intraocular pressure reached 25 mm. Hg, without showing any further rise; they assumed that the aqueous humor, streaming under higher pressure, was able to find a new way by overcoming the pressure present in the deep ciliary veins, which are said to have higher intravascular pressure than the superficial ciliary veins. In this interpretation, a difficulty is involved: Between the superficial and the deep ciliary veins numerous intrascleral anastomotic connections are known to exist, and the two groups have the same final drainage. If the assumption of Weekers and Prijot were justified, a retrograde blood flow might be expected in the epibulbar veins, even under normal circumstances.

De Vries described spontaneous changes in the aqueous flow from one Ascher vein into one recipient vein or another. Similar observations were made during compression of the eyeball; this may simulate a backflow phenomenon in a recipient vein or in an aqueous vein at its exit from a scleral emissary. Caution is necessary in order that the change in direction from one epibulbar vein to another be not mistaken for a real backflow phenomenon.

The objection could arise that during the compression test the eyeball is being pressed against the bony wall of the orbit and thus a local obstacle may be introduced into the current in epibulbar veins; this objection can be refuted by the fact that the backflow phenomenon occurs also in veins which, because of their location on the eyeball, cannot possibly become pressed against the orbital wall. Eyes showing the backflow phenomenon at pressure values of only 30 gm. exhibited the phenomenon irrespective of whether the pressure was applied to the sclera or to the corneal center; with pressures higher than 30 gm., the dynamometer slides away from the corneal center.

2. During compression of the eyeball an increase in pressure inside the episcleral veins produces the backflow phenomenon in the aqueous veins. This effect is favored by the increased pressure in epibulbar veins during the increasing phase of the pressure in glaucomatous eyes, as described by Thomassen.

13. Lindner, K.: Personal communication: Sitzungsb. Wien. ophth. Gesellsch. Nov. 1950.

14. Weekers, R., and Prijot, E.: Recherches expérimentales sur les fonctions des veines aqueuses, Ophthalmologica **119**:321, 1950.

It seems that the reversal of flow is restricted to aqueous veins and their recipient vessels. During compression of the jugular veins with a rubber cuff, all episcleral veins, as well as the aqueous veins, show stasis; aqueous veins may even show a slow retrograde flow. This can be explained by the fact that the aqueous veins lack any proximal capillary network, whereas the capillary network of regular veins does not permit such a backflow. After studying the stasis in epibulbar veins of glaucomatous patients subjected to compression of the jugular vein, I have reached the preliminary conclusion that in glaucomatous eyes the stasis occurs at lower levels of compression than in normal eyes.

3. During compression of the eyeball, the pressure in the aqueous veins drops below the level of the pressure in epibulbar veins, owing to interference with elimination of aqueous humor from the canal of Schlemm; this facilitates the retrograde blood flow into the aqueous veins. Goldmann found that the amount of fluid leaving Schlemm's canal in glaucomatous eyes was not higher than the amount leaving eyes with normal pressure; he assumed an impediment at the level of the trabeculum corneosclerale (ligamentum pectinatum). We do know, however, that, at least in less far-advanced glaucoma, the increased resistance to aqueous flow cannot be due to a histologically definite, irreversible change in the trabecular meshwork. This consists mainly of collagenous, and also elastic, fibers. An increased resistance in this region most probably is due to a change which is not permanent and which can be influenced pharmacologically. The openings permitting the entrance of aqueous humor into the canal of Schlemm might be subject to an increased water content of the surrounding collagen fibrils, rather than to sclerosis or to pigment infiltration of the pectinate ligament, which would permit neither rapid oscillations in pressure in glaucomatous eyes nor a speedy drop of intraocular pressure after medication.

One might assume that this imbibition of the fibrils is caused by chemical changes in the aqueous humor and that opposite changes will produce dehydration of these fibers, and thus facilitate the elimination of aqueous humor. I shall not discuss whether changes in hydrogen ion concentration or in the electrolyte content may be a decisive factor.

The assumption of cellular imbibition in the pectinate ligament could explain why in glaucomatous eyes less aqueous humor would enter the outlets of Schlemm's canal during compression of the eyeball. It is understandable that mechanical pressure of the hydrated fibrils could produce a more or less inpenetrable impediment between the anterior chamber and Schlemm's canal; it is also understandable that during bulbar compression stasis occurs as soon as the compensation maximum is reached. This is because then no further fluid leaves the canal of Schlemm. Not explained by this assumption is the retrograde blood flow in the aqueous veins: Is it a washing out of the aqueous humor by entering venous blood? Such an explanation would agree with the observation that the backflow of blood lasts only until the aqueous vein is completely filled with blood. Aqueous humor will not be forced back into the anterior chamber because of the much higher pressure prevailing in the chamber. Another solution would be the assumption that some aqueous humor remaining in Schlemm's canal after cessation of free aqueous-humor circulation

will be evacuated through the posterior ciliary veins. A condition for both of these assumptions is that as soon as the compensation maximum is reached, little or no more aqueous humor is eliminated.

It is difficult to say how far these observations parallel Ascher's "negative glass-rod phenomenon"; in this instance, also, it is questionable whether during the blood-influx phenomenon aqueous humor is being pushed away by the entering blood or whether it is only washed out. It may be stated that during compression of the eyeball in normal eyes the blood-backflow phenomenon will be observed only as an exception, while Ascher's blood-influx phenomenon occurs in about 50% of all normal eyes.

In this connection, it should be mentioned that in ocular diseases leading to increase in intraocular pressure, and obviously connected with chemical changes in the aqueous humor, i. e., in secondary glaucoma, the eyeball-compression test almost always produces the reversal of flow in the aqeuous veins. The compensation-maximum readings were also low in some cases of iritis not complicated by an increase in ocular pressure; in these cases secondary glaucoma does not occur, probably because of the marked reduction of the total fluid transfer, i. e., decrease in the amount of fluid produced, as well as eliminated.

Huggert [15] made similar observations when studying the effect of naphazoline (privine®) on secondary glaucoma: Before treatment with naphazoline, pressure exerted upon the eyeball produced an influx of blood into the aqueous veins; when the intraocular pressure was normalized after administration of naphazoline, compression of the eyeball did not produce influx of blood into the aqueous veins. Huggert drew a parallel between his observations and Ascher's blood-influx phenomenon; I believe that Huggert observed the same blood-backflow phenomenon which occurs in aqueous veins during performance of the compensation-maximum test.

SUMMARY

I observed that in eyes with glaucoma, of different types, a retrograde influx of blood from episcleral veins into aqueous veins occurred during compression of the eyeball (backflow phenomenon). The dynamometer pressure necessary to produce this phenomenon was termed "compensation maximum." In eyes with normal pressure, compression up to even 150 gm. usually would not produce the backflow phenomenon into aqueous veins, while the compensation maximum of glaucomatous eyes in many instances was found to be below 100 gm. It seems that the appearance of the backflow phenomenon into aqueous veins is conditioned upon an interference with aqueous-humor elimination. Compensation-maximum readings proved helpful for clinical clarification of suspected cases of glaucoma. The possible explanations of backflow phenomenon and obstruction to elimination are discussed.

II. Univ. Augenklinik., Vienna IX, Alserstr. 4, Austria.

Dr. K. W. Ascher, of Cincinnati, gave helpful advice in the translation of this paper.

15. Huggert, A.: Use of Privine as a Pressure-Reducing Medium in Iridocyclitis Glaucomatosa, Acta ophth. **28**:393 1950.

DARK ADAPTATION IN PERIMETRICALLY BLIND FIELDS

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THE COMMONLY accepted theory of dark adaptation relates the threshold for light perception to the concentration of visual purple in the retina.[1] The arguments that the retina is the major, if not the only, site of the dark-adaptation process are based on deductions made from measurements of dark adaptation, brightness discrimination, flicker perception, and retinal photochemistry. Little consideration has been given to the role of the central nervous system (retinogeniculocalcarine system) in dark adaptation. Attempts to analyze the dark-adaptation process into its component parts have been mainly chemical. These studies have provided a detailed knowledge of the photochemistry of the retina and a description of a mechanism capable of absorbing light energy and then releasing the energy needed to begin the train of nervous impulses. Comparison of the in vitro behavior of retinal chemical reactions and the dark-adaptation process, as measured by Hecht's method, showed that their activities were parallel when expressed in terms of change as a function of time. Thus, Hecht proposed [2] that the dark-adaptation curve was a direct expression of the reversible photochemical reaction in the retina. From this it followed that dark adaptation could be adequately described as a process whereby visual sensitivity to light increased as the concentration of the photochemical substance increased. This implied a direct one-to-one relationship between the stimulus and the sensory effect; that is, a certain amount of light energy effected a specific amount of chemical change, thereby liberating a specific amount of nervous energy and inducing a specific amount of sensory effect.[3]

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1. (*a*) Craik, K. J. W., and Vernon, M. D.: Nature of Dark Adaptation, Brit. J. M. Psychol. **32**:62, 1941. (*b*) Granit, F.; Munsterhjelm, A., and Zewi, M.: Relation Between Concentration of Visual Purple and Retinal Sensitivity to Light During Dark Adaptation, J. Physiol. **96**:31, 1939. (*c*) Lythgoe, R. J.: Mechanism of Dark Adaptation: A Critical Resumé, Brit. J. Ophth. **24**:21, 1940.

2. Hecht, S.: (*a*) Intensity Discrimination and the Stationary State, J. Gen. Physiol. **6**:355, 1924; (*b*) Visual Discrimination of Intensity and the Weber-Fechner Law, ibid. **7**:235, 1924; (*c*) Nature of the Visual Process, Bull. New York Acad. Med. **14**:21, 1938.

3. Hecht, S.: Dark Adaptation of the Human Eye, J. Gen. Physiol. **2**:49, 1919-1920.

The objections to this hypothesis are many. Crozier [4] pointed out that the form of the dark-adaption curve need not be considered the expression of a photochemical reaction in the retina. He proposed, instead, that the form of this curve may be accounted for in terms of the number of neurons available at any given time within the entire visual pathway. Such a concept made it unnecessary to assume that the sensory effect for a threshold event is constant or has a fixed relation to a constant amount of photochemical change. In addition, Granit and associates [1b] have shown that there is a discrepancy between the actual amount of photochemical substances found in the retina and the degree of dark adaptation at the end of this process. Thus, there is a question whether the process of dark adaptation is determined only, or in major part, by a peripheral mechanism, such as retinal photochemical changes.

One reason for most of the emphasis on the retina is that there have been few studies of dark adaptation subsequent to changes in the brain. Earlier work by one of us [5] and that of other investigators [6] have shown that varying the concentration of carbon dioxide and of oxygen in the inspired air will alter dark adaptation. Changes in concentration of these gases affect not only the retina but cerebral function as well. Therefore, the alterations in dark adaptation thus produced might be due to dysfunction either in the retina or in the cerebrum or in both.

Investigations of changes in dark adaptation as result of lesions in the brain were carried out by Ullrich.[7] He described 15 cases of penetrating shrapnel wounds of the occiput. All his patients experienced visual phenomena known to be associated with lesions of the occipital lobe. At the time of examination, two of his patients had bilateral inferior altitudinal hemianopsia, two had bilateral subcentral scotoma, one had a minimal binasal defect, and one had recovered from a homonymous hemianopsia. The other nine at no time had a demonstrable field defect. After light-adapting his patients, Ullrich measured the time until a small black cross would be seen upon a background of given intensity. Fixation was bilateral. He thus arrived at a curve which in some senses measured dark adaptation.[8] When he compared the curves of the patients with those of the normal

4. Crozier, W. J., and Morgan, U.: On Auditory Intensity Discrimination, Proc. Nat. Acad. Sc. **23**:417, 1936. Crozier, W. J.: Theory of the Visual Threshold: I. Time and Intensity, ibid. **26**:54, 1940; Theory of the Visual Threshold: II. Kinetics of Adaptation, ibid. **26**:334, 1940.

5. Wald, G.; Harper, P. V., Jr.; Goodman, H. C., and Krieger, H. P.: Respiratory Effects upon Visual Threshold, J. Gen. Physiol. **25**:891, 1942.

6. Bunge, E.: Verlauf der Dunkeladaptation bei Sauerstoffmangel, Arch. Augenh. **110**:189, 1936. McDonald, R., and Adler, F. H.: Effect of Anoxemia on the Dark Adaptation of the Normal and of the Vitamin A-Deficient Subject, Arch. Ophth. **22**:980 (Dec.) 1939. McFarland, R. A., and Forbes, W. H.: Effect of Variations in the Concentration of Oxygen and Glucose on Dark Adaptation, J. Gen. Physiol. **24**:69, 1940-41.

7. Ullrich, N.: Adaptationsstörungen bei Sehhirnverletzten, Deutsche Ztschr. Nervenh. **155**:1, 1943.

8. This method, however, did not measure the absolute threshold, i. e., the smallest amount of light required to just appreciate the difference between absolute darkness and light at any given time. What was probably measured was a difference threshold, i. e., the smallest difference in illumination necessary to just allow the black cross to be distinguished from the background. This is probably why Ullrich's normal curves did not exhibit the plateau which appeared in Hecht's determinations, and which has been correlated with the change from photopic to scotopic vision during the process of dark adaptation.

subjects, he found adaptation to proceed more slowly and to a less complete degree in the abnormal subjects. This observation he interpreted as indicative of altered dark-adaptation processes following lesions in the brain but not the retina. Ruesch [9] studied a group of subjects with the biophotometer, an instrument which only approximately measures the absolute threshold. He examined his patients after 10 minutes in the dark, then after 5 minutes of exposure to light, and then for about 10 minutes in the dark again, thus determining a pattern of visual-threshold changes. Data for normal controls were not presented, but correlation with the other visual tests (for which control data were presented) led Ruesch to suggest that head or brain injury affects dark adaptation. Again, this work is only suggestive of such an effect.

Our own investigations describe dark-adaptation curves derived from measurements of the serial changes in the absolute threshold of patients with lesions in the visual pathways beyond the retina.[10] Our data indicate that alterations in dark adaptation may be produced by lesions in the brain while the retina remains intact.

MATERIAL

The subjects studied were the same as those reported in a previous communication.[10] They all had defects in their fields of vision, as determined by routine perimetry under standard light conditions. Table 1 presents the pertinent historical data and a summary of the perimetric examinations for this group. All these patients had normal retinas. Routine perimetric examination under 7 foot-candles (f.-c.) of illumination showed homonymous or heteronymous defects. These patients, when examined with a luminous target in a dark room, saw the target within the apparently blind field. Thus, under proper conditions the so-called anopic areas were responsive to light stimuli. There were appreciation of light, appreciation of changes in intensity, appreciation of movement, formation of after-image, and ability to localize the target in these regions. It was considered that these visual sensations may have been artefacts due to entoptic stray light and retinal neural interaction. However, the available facts seemed to exclude the artefacts. It was thought that the findings indicated the presence of some function in these apparently "anopic" areas.

METHOD

At first the visual fields were determined under an illumination of 7 (f.-c.). Later the patient was light-adapted. Immediately after this, the room was completely darkened, and serial absolute-threshold measurements were made at a specific locus in the visual field. The target was transmitted light, exposed for 1/25 second. The source of light was essentially Wald's portable adaptometer,[11] so modified that the luminous target, a circle subtending 2.5 degrees of retinal angle, could be placed at any visual angle along any meridian of the patient's field at a distance of 27 cm. from his eye. With this apparatus, the intensity of the source of light was controlled by varying the current flowing through the lamp.[12] Ocular fixation was maintained by the subject looking at a pinpoint of red light always kept just visible. The head was fixed to the perimeter. Precautions were taken to eliminate extraneous clues by presenting the

9. Reusch, J.: Dark Adaptation, Negative After-Images, Tachistoscopic Examination and Reaction Time in Head Injuries, J. Neurosurg. **1**:243, 1944.

10. (*a*) Krieger, H. P., and Bender, M. B.: Dark Adaptation in Lesions of the Optic Pathways, abstracted, Federation Proc. **8**:89, 1949. (*b*) Bender, M. B., and Krieger, H. P.: Visual Functions in Perimetrically Blind Fields, A. M. A. Arch. Neurol. & Psychiat. **65**:72, (Jan.) 1951.

11. Wald, G.: Portable Visual Adaptometer, J. Optic. Soc. America **31**:235, 1941.

12. This method introduces a spectral change at low intensities. The addition of neutral filters made the use of low intensities unnecessary and so partially overcame this. However, as will be seen, the difference in threshold between the normal and the defective fields was so great that the slight spectral shift became insignificant.

target in a homogeneous, black, nonreflecting field in the otherwise absolutely dark room. The pupils were not treated with drugs, and one eye was covered with a patch while the other was being examined.

Prior to the study of each patient in darkness, he was light-adapted for five minutes with 1,500 millilamberts (ML) diffused over a monocular field subtending 50 degrees of retinal

TABLE 1.—*Pertinent Perimetric and Historical Data*

Case	Age, Yr.	Perimetric Fields	Clinical History
A. F.	39	Left homonymous hemianoptic defect with 8° macula sparing	Right occipital subdural hematoma; paresis of right third nerve (transient) Cause: presumably traumatic
M. F.	42	Left homonymous hemianoptic defect with 5° macula sparing	Right subdural hematoma, with transient, mild, right-sided paresis and bilateral hyperreflexia Cause: never clearly established; patient known to be alcoholic, with rheumatic heart disease and signs of subacute bacterial endocarditis
A. M.	29	Bitemporal heteronymous hemianopsia with binasal 8° ring scotomas and 5° macula sparing	Six years of progressive visual difficulty, especially with night and color vision Pneumoencephalography failed to reveal any chiasmal pathology; defect in color vision when tested with pseudoisochromatic cards
E. G.	72	Right homonymous hemianopsia with 5° to 8° macula sparing	Elements of aphasia; occasional periods of confusion; no paresis, but episodes of unconsciousness with falls leading to mild trauma; hemianopsia following one such episode Cause: patient died of condition diagnosed as chronic hypertensive arteriosclerotic heart disease; no autopsy
M. E.	18	Right homonymous hemianopsia with 15° to 20° macula sparing	Sudden onset of homonymous hemianopsia, unaccompanied by other signs or symptoms Cause: unknown
H. G.	66	Bilateral, almost complete homonymous, anopia with some vision remaining to either side of midline of inferior quadrants of both visual fields	Sudden onset of dizziness, blindness, and nonpsychotic visual hallucinations in 1944; mild improvement in vision Cause: unknown
S. R.	30	Left peripheral homonymous hemianoptic field defect, which cleared spontaneously	Rheumatic heart disease in childhood; in 1947, hemoptysis and transient left hemiparesis; in 1949, left hemiparesis reprecipitated by carbon monoxide poisoning, accompanied by left hemisensory syndrome with hemianopsia; gradual, incomplete recovery in all spheres, but no apparent visual defect remaining
B. L.	47	Bitemporal defect, hemianoptic in left eye but irregular in right eye	Optic nerve atrophy and signs of pituitary tumor
S. C.	28	General constriction, most marked in three quadrants	Brain injury with shrapnel in occipital areas; hemianopsia, mild memory defect, slight aphasia, general intellectual slowness; defect in color vision demonstrated with pseudoisochromatic cards
M. M.	18	Homonymous hemianopsia; spontaneous recovery	Sudden onset of diplopia followed by hemianopsia Cause: congenital syphilis Complete remission during therapeutic course; mild exacerbation 2 mo. later

angle. Immediately after the five-minute period, the light-adaptation source was turned off, and the patient looked at the fixation point. Thereafter he began to expose the target to himself as fast as he found convenient, until he first became aware of any light in addition to the fixation point. This procedure was repeated many times until the dark-adaptation process had ceased for all practical purposes. Most patients exposed the target about once every two seconds. The time between beginning any one determination and reaching the threshold was under the control of the experimenter.

This is essentially the method Hecht and Schlaer [13] used to measure dark adaptation. It allows the absolute visual threshold to be measured at any time during the dark-adaptation process, since for each determination the experimenter gradually increases the source of illumination until it just becomes visible. A light exposed for 1/25 second at this intensity does not appreciably affect the dark-adaptation process. If these absolute thresholds are graphed as a function of time, the dark-adaptation process may be represented by a dark-adaptation curve. Such curves were constructed for the normal and the defective fields of the patients. Because it took about an hour to measure the adaptation process for any given area at any one sitting, it was decided to sample the fields of each patient. Most of the measurements were made along the four principal 45-degree meridians of the field of vision at 10, 20, 30, and 45 degrees of retinal angle from the fixation point. In addition, the adaptation process was measured at 5 degrees directly below the fixation point and, in a few cases, at the fixation point. In most cases over 20 curves were constructed for each eye. For the construction of each curve about 45 threshold determinations were made during the 40 to 50 minutes over which adaptation took place. Each point examined in a defective field was studied at least twice. For the analogous normal point one curve was determined. In our investigations the threshold was measured in micromillilamberts (brightness) of the just visible target and expressed in logarithmic units. Time was expressed in minutes.

A comparison of the dark-adaptation curves of the perimetrically normal and the perimetrically defective field of the same patient then enabled a quantitative and qualitative statement of the difference between the normal and the abnormal part of the field of vision to be made. Such a comparison allowed the perimetrically normal parts of a monocular field of vision to act as the control for the defective parts of the same field. A further control was afforded by a comparison of the defective areas of each eye of one patient.

RESULTS

Hundreds of absolute visual threshold measurements were made for both the perimetrically normal and the perimetrically defective visual fields. The results of repeated threshold determinations over a period of 2 to 16 months were the same. In the perimetrically normal areas of our patients the thresholds and dark-adaptation curves were the same as those found for normal subjects by Hecht and associates [14] and by Mandelbaum.[15]

Comparison of the thresholds and curves of the normal fields and those of the defective fields brought out a number of differences. First, there was a rise in the absolute visual threshold throughout the course of dark adaptation. This is illustrated in Figure 1, which presents the perimetric fields and corresponding dark-adaptation curves of patient M. F. The onset of adaptation proceeded too rapidly for an accurate comparison of thresholds at this phase of the process. However, the thresholds in the abnormal fields at the beginning of adaptation were, on the average, 200 times as high as in analogous normal loci. Between the onset and the end of adaptation this threshold difference was maintained or increased. At the end of adaptation, when the curve was flat and the threshold difference therefore most easily determined, the threshold in the case of M. F. was 200 to 900 times higher in the abnormal fields. Table 2 contains the average log-

13. Hecht, S., and Schlaer, S.: An Adaptometer for Measuring Human Dark Adaptation, J. Optic. Soc. America **28**:269, 1938.

14. Hecht, S.; Haig, C., and Wald, G.: Dark Adaptation of Retinal Fields of Different Size and Location, J. Gen. Physiol. **19**:321, 1935-1936.

15. Mandelbaum, J.: Dark Adaptation: Some Physiologic and Clinical Considerations, Arch. Ophth. **26**:203 (Aug.) 1941.

arithmic values of the absolute visual threshold at the end of adaptation for eight representative points in the visual fields of the patient M. F. A similar order of threshold differences between analogous points within normal and defective fields was also found in the other patients. In all the patients this threshold difference was always so great that any given pair of analogous dark-adaptation curves never crossed each other.

A second difference noted between the normal and the defective visual fields was the greater degree of fluctuation of the absolute visual threshold in the defective fields. For example, in the case of M. F., after adaptation had ceased, the fluctuation in the threshold of the normal field was never more than 0.4 log unit (2.5 μmL). In the analogous defective field this fluctuation was as great as 1.0 log unit (10 μmL). Thus, there was a fourfold increase in the degree of fluctuation or instability of this threshold in the perimetrically defective areas.

A third difference between the normal and the defective fields was found in the shape of their dark-adaptation curves. The curves of the two types of fields

TABLE 2.—*Average Absolute Visual Threshold at Completion of Adaptation and Corresponding Threshold Difference at Eight Representative Loci of the Visual Fields of M.F.**

Left Eye		Right Eye	
Left Upper Quadrant	Right Upper Quadrant	Left Upper Quadrant	Right Upper Quadrant
5.17	2.45	5.20	2.83
Difference 513 times		Difference 235 times	
Left Lower Quadrant	Right Lower Quadrant	Left Upper Quadrant	Right Upper Quadrant
5.50	2.55	5.60	2.90
Difference 282 times		Difference 501 times	

* Each measurement was made at 20 degrees of arc along the 45-degree meridian of the indicated quadrant of the visual field. Thresholds are expressed in logarithmic units of micromillilamberts.

were not parallel. This difference does not allow a statement as to comparative differences in the over-all rate of adaptation of the normal and the abnormal fields. However, the curves of Figure 1 show three significant comparative differences: (*a*) In the abnormal areas the initial rapid period of adaptation characteristic of the normal areas was absent; (*b*) in the abnormal areas it took longer for a given fall in threshold to occur than it did in the normal areas; (*c*) in the curves of the abnormal areas one point of change in rate of adaptation (with an occasional suggestion of a second) was found, whereas the curve of the normal areas had three. These three points of change in rate of adaptation in the normal curve produced a plateau which has been interpreted by most investigators as the final threshold of cone function. The fall in threshold thereafter has been considered the subsequent adaptation of the rods alone. In the curves of the abnormal areas there was no clear-cut indication of such a plateau. However, whereas the normal curves exhibited a sharp initial drop, the abnormal curves sometimes began with a gentle slope, which increased a little before becoming parallel to the abscissa.

Comparison of the curves of the normal and the defective fields showed one similarity. The total range of adaptation was of the same order for the two i. e.,

about 3.6 log units. In the cases of bilateral visual field disturbances, the total range of adaptation varied from 3.5 to 4.0 log units. In these cases there could not be the control in the form of a normal analogous field, but the range of adaptation was the same as that for the hemianoptic eye. Mandelbaum, using essentially the same technique in 110 normal subjects, also found the total range of adaptation to vary from 3.5 to 4.0 log units.[15]

Thus, comparison of the adaptation curves of the normal and the abnormal areas showed (1) that adaptation took place in the abnormal areas, but (2) that the absolute threshold for vision was always higher in the abnormal areas; (3) that adaptation was slower in the abnormal areas; (4) that the total range of adaptation was the same in the both areas; (5) that the adaptation curves of the abnormal areas had a somewhat different shape from the normal curve[16]; (6) that, although there were differences in threshold between various parts of a defective field, these differences were never as great as those between a defective locus and its analogous control.

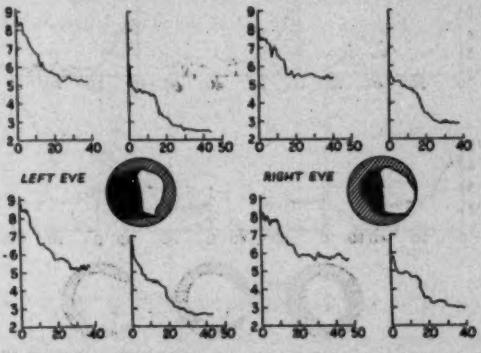

Fig. 1.—Dark-adaptation curves of M. F. The perimetric fields of vision under daylight illumination show homonymous hemianopsia, indicated by the blacked-out regions. Four sample curves are presented for each eye, each curve being measured at 20 degrees of retinal angle along the 45 degree meridian of each quadrant.

On the abscissa is represented time in minutes; on the ordinate, the logarithm of the visual threshold, expressed in micromillilamberts.

Note that the thresholds of the defective homonymous half-fields are higher than those of the normal homonymous half-fields.

These generalizations applied to the six patients with hemianopsia. In the three patients A. M., S. C., and H. G. there was more than a hemianoptic defect, thereby eliminating a control in the form of a normal half-field. However, when the curves of these patients' defective fields were compared with our normal curves and with those of Hecht and his followers, it was found that our generalizations still held true.

The case of S. R., who recovered from a homonymous hemianopsia with residual defects in the periphery of the affected half-fields of vision, afforded additional observations in regard to the fluctuation of the threshold in defective visual fields.

16. The apparent lack of a cone hump was noted at 10 degrees, as well as at 20 degrees, from the fovea.

As already noted, these thresholds exhibited greater fluctuation than those of corresponding normal areas, and this fluctuation became especially evident at the end of adaptation.

It will be recalled that the difference among the defective final thresholds was as great as 1.0 log unit, whereas the greatest difference among the normal final thresholds was 0.4 log unit, thus giving an indication of the size of the increased oscillation. The case of S. R. conspicuously illustrates this fluctuation, which here occurred without a concomitant rise in threshold in the perimetrically defective area. In Figure 2 will be found the dark-adaptation curves of this patient measured at various intervals during the recovery period at one locus [17] in the defective field. When the perimetric defect was large, the fluctuation was great, although the threshold was not elevated; as the defect decreased, the degree of threshold fluctuation subsided. Ultimately, the normal and previously defective area appeared alike perimetrically and in dark-adaptation studies.

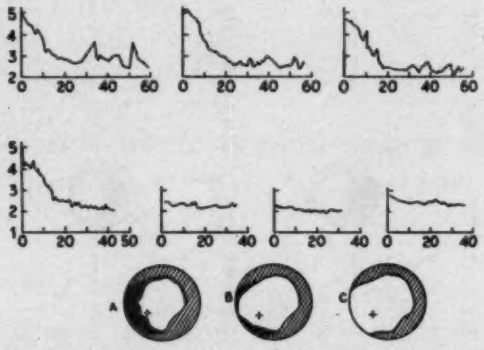

Fig. 2.—Absolute visual threshold and perimetric fields of S. R. The visual fields were charted during the period of recovery, indicated at *A*, *B*, and *C*. Blacked-out areas indicate defective parts of the perimetric field of vision in daylight illumination. The + indicates the region at which the absolute visual threshold was measured at various times during the course of recovery over a period of weeks. The last three curves represent only the final stages of dark adaptation. Note the decrease in the degree of fluctuation in the visual threshold as recovery progressed. Coordinates are the same as those in Figure 1.

The case of M. M. was of particular interest because we examined this patient shortly after the onset of the hemianopsia and studied her repeatedly until her complete recovery. During the existence of the hemianopsia, the dark-adaptation curves of the defective areas resembled those found in the other cases of hemianopsia and covered the same ranges of intensity. The only difference was noted in the presence of a plateau during the second and third minutes of dark adaptation. This was suggestive of a cone plateau. Dark-adaptation measurements made two days after spontaneous, and subjectively sudden and entire, recovery from the hemianopsia showed the threshold to have fallen to within the range of normal, but with

17. Since this locus was well outside the area of cone vision, the cone plateau is not present in these dark-adaptation curves.

increased fluctuation, while the dark-adaptation curve showed a more definite cone plateau. A third curve, made one week after recovery, was normal as compared with the curve for the nondefective field and with those for other normal fields. The decrease in threshold fluctuation is reminiscent of the observation that a partial defect is more apt to fluctuate than either the normal condition or a complete defect. In a sense, this case summarized the results of our study. During the period when there was a hemianopsia, the dark-adaptation curve showed a rise in threshold of over 300 times and an increased fluctuation. Shortly after spontaneous recovery, at which time there was no perimetric defect, the dark-adaptation curve showed only abnormal irregularities. Subsequently, the adaptation curve became normal.

A somewhat different type of field defect was found for A. M., who had a bitemporal hemianopsia and an additional binasal ring scotoma. His fields were sampled at many points. In general, it was found that the absolute visual threshold was raised in those areas which were defective on perimetric examination. In Figure 3 will be found the absolute visual thresholds at the end of adaptation for various points of the visual fields of A. M. It is of particular interest to note

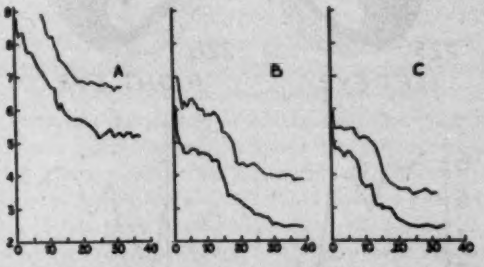

Fig. 3.—Dark-adaptation curves measured with a 2.5-degree luminous target, indicated by the thick line, and 40-minute target, indicated by the thin line. All curves were measured at 20 degrees of visual angle along the 45-degree meridian of specified quadrants of the visual field. Curves *A* were measured in the perimetrically defective half-field of vision of M. F.; curves *B* were determined in the normal half-field of the same patient; curves *C* were measured in the field of vision of a normal subject. Coordinates are the same as those in Figure 1.

that our method of examination allowed the demonstration of differential thresholds across the scotomas found in this patient.

One final set of observations should be considered. It has been demonstrated, in the normal, that reduction in the size of the target induces a general rise in the threshold, reflected as an elevation of the dark-adaptation curve on its ordinate. We also found this to be true when a target subtending 40 minutes of retinal angle was used in place of the target subtending 2.5 degrees. Figure 4 presents the curves of the patient M. F. arrived at with these two targets for both a normal and a defective area. In addition, similar curves of a normal subject (R. P.) are presented for comparison. In the patient, use of the 40-minute target raised the threshold 1.5 log units in both the normal and the defective areas. In the normal control the rise was 1.0 log unit. Unfortunately, our target had a limiting brightness of $\log_{10} 9$ μmL, thus making it impossible, with the small target, to construct a complete curve for M. F.'s defective area. However, one important observation

was made with the 40-minute target; mere reduction in the size of the target did not effect a loss of the cone plateau in the normal curve. The only change noted for the normal was a general rise of threshold. This would make it appear that both the normal and the abnormal respond only with a rise in threshold when the target is reduced.

CONCLUSION

In an earlier communication,[10] the qualitative aspects of perception of luminous targets within hemianoptic fields under conditions of darkness were described, and the validity of these perceptions was considered in detail. Although it is difficult to explain these phenomena, the fact remains that luminous targets can be perceived and localized, provided the background illumination is low or absent, in those parts of the field found to be blind by routine perimetric examination. The present study

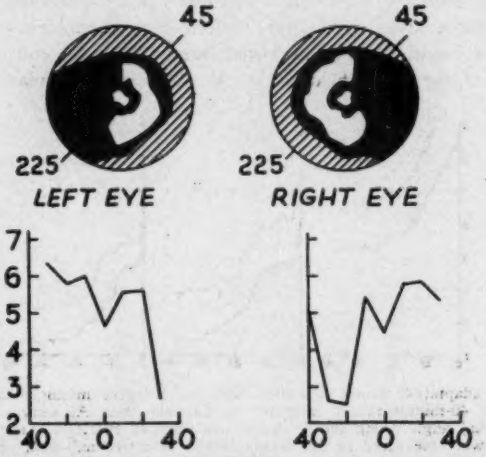

Fig. 4.—Absolute visual thresholds for various points in the fields of vision of A. M. The perimetric fields were plotted under 7 f.-c. of illumination. The absolute visual thresholds in darkness were determined after 30 minutes of dark adaptation for various retinal points along the 45- to 225-degree meridian of each eye. These are indicated in the curves plotted below each field of vision. Note the rise in threshold values measured in the defective areas, including the ring scotomas. On the abscissas are represented degrees of retinal angle along the 45- to 225-degree meridian; on the ordinates, logarithms of the visual threshold, expressed in micro-millilamberts.

showed that, under conditions of darkness, the changes in the absolute visual threshold could be measured for these fields and that from such measurements it was possible to construct dark-adaptation curves. Since the lesions in our patients were in the brain or the optic chiasm and the retinas appeared normal, it must be concluded that the alterations in adaptation were not due to disturbances in the photochemistry of the retina.

The meaning of our results in terms of Hecht's photochemical concepts is not entirely clear. In his 1937 Harvey Lecture,[2c] he stated that all parts of the visual system and the effector system contribute to the final perceptual-behavioral act

called seeing. But he pointed out, as Adrian had shown,[18] that the end-organ "fatigues" more rapidly than the nerve. Thus, the end-organ becomes a limiting factor, and its physiological reaction may determine both the qualitative and the quantitative aspect of any measurements, completely masking effects contributed by those parts of the system fired off by the end-organ. It is as though the end-organ acted as a pacemaker. So Hecht concluded that his photochemical analysis of the visual process was warranted and did not contradict the concept that the central nervous system affects dark adaptation. If this line of thought is adhered to, how shall we interpret the changes found subsequent to lesions affecting the central nervous system but not the retinas? It may be that the lesion has a retrograde effect upon the end-organ and its photochemistry. However, it seems more attractive to accept the "pacemaker" concept and postulate that the lesion so changes the relationship between the end-organ and the rest of the visual system as to make the central parts the limiting factor instead. Should this turn out to be so, then, although Hecht's theories might hold true for the normal, a new concept of dark adaptation will be needed for the injured brain in which the retinal photochemistry is unaltered.

Our work also indicates that dark adaptation, the measurement of which is dependent upon a behavioral response, may change, although the retinal photochemistry apparently does not. This investigation does not support the assumption of a direct one-to-one relationship of the light stimulus, the photochemical process, and the sensation of vision. Such an assumption precludes an active role of the central nervous system in the process of adaptation. Our data show that lesions of the central nervous system actively influence the dark-adaptation process.

The adaptation changes which we found for the abnormal fields might be interpreted by some as merely a rise in threshold due to a conduction block in the visual pathways. If this were so, then the abnormal curves would be expected to have the same shape as normal curves, and merely to be raised on the intensity axis. However, this was not the case. In addition to the rise on the intensity axis in the abnormal areas, there was a decrease in the rate of dark adaptation.

Moreover, the cone plateau of the normal curves was not found in the abnormal curves. Further work is required to interpret fully this lack of a cone plateau. But the curves found by using the 40-minute target instead of the 2.5-degree target showed that for the normal areas a rise in threshold was not accompanied by a change in the shape of the dark-adaptation curve or by a loss of the cone plateau. These observations indicate that a lesion in the central nervous system not only alters dark adaptation by raising the threshold and increasing its instability but also affects its qualitative aspects. An analogous situation exists in the comparison of the changes in adaptation in cutaneous sensation as a result of lesions of the peripheral nerve and the changes resulting from lesions of the parietal lobe. In lesions of the parietal lobe the cutaneous sensory adaptation time is altered much more than in lesions of the peripheral nerve. This difference has been interpreted as indicative of the action of the central nervous system in adaptation processes, even though in each case a conduction block was produced by the particular lesion.[19]

18. Adrian, E. D.: The Basis of Sensation. The Action of the Sense Organs, New York, W. W. Norton & Company, 1928.

19. Bender, M. B.: Changes in Sensory Adaptation Time and After-Sensation with Lesions of Parietal Lobe, Arch. Neurol. & Psychiat. **55**:299-319 (April) 1946.

SUMMARY

The use of Selig Hecht's dark-adaptation technique for the examination of patients with visual field defects as a result of lesions of the optic pathways yielded the following results:

1. Scotomatous areas as determined by routine perimetry may reveal the presence of visual function when tested under the condition of total darkness.

2. The absolute threshold of this visual function for these areas could be measured.

3. Measurement of dark adaptation in these parts of the field of vision yielded data from which dark-adaptation curves could be constructed.

4. These curves differed from the normal in that (*a*) they were raised on the intensity axis, indicating a general rise in threshold, (*b*) they did not show the points of inflection found in the normal curve, commonly associated with the change from cone to rod function, (*c*) they showed an increased fluctuation in the absolute visual threshold, and (*d*) they gave some indication that dark adaptation proceeds at a slower rate in defective areas.

5. During the restitution of visual function in these abnormal areas, the dark-adaptation curves approached those found in the normal.

The significance of these observations in relation to the photochemical theory of dark adaptation is discussed.

SOME AIDS IN OPHTHALMOSCOPY

Contact Glass; Transilluminating Procedures; Headlight Employed as Ophthalmoscope

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PROVIDENCE, R. I.

IN DIFFICULT cases of disease involving the ocular fundus the use of several methods of examination may at times be of value in arriving at a reasonably exact diagnosis. The following procedures have been found to be of value in such instances, particularly in those of retinal detachment and of fundus tumor.

USE OF CONTACT LENS OF TRONCOSO WITH DIRECT OPHTHALMOSCOPY FOR OBSERVATION OF PERIPHERAL FUNDUS

In the examination by direct ophthalmoscopy of the fundus of an eye with little astigmatism and with clear media, the clear, sharp image of the posterior pole gives way peripherally to an increasingly blurred and distorted picture. The most peripheral portion of the observable fundus shows merely as a reddish-orange blur, in which only very large or very prominent lesions, if present, can be seen. Schepens [1] has recently commented on this subject in his valuable studies of the peripheral retina in cases of detachment.

If one examines the emmetropic eye with the retinoscope, not in the visual axis, but at an angle to it, i. e., in the direction in which one looks in order to observe the peripheral fundus, two major differences from the picture with ordinary retinoscopy, in the visual axis, appear. First, of course, the pupil is now oval, owing to the oblique axis of observation; and, second, a meridional scissors movement is noted. Approximately 8 D. in difference is present between the "with" and the "against" component of the scissors movement. Should one now examine retinoscopically the periphery of the aphakic eye, using corrective lenses, the same aberration is found to exist in approximately the same degree, it being taken into account that higher plus lenses are needed to neutralize the aphakic eye. Jackson [2] commented on this phenomenon in 1897, when he stated that cases in which scissors movement appeared with retinoscopy belonged to the category of irregular astigmatism and that the phenomenon could be observed in most normal eyes if the shadow test was performed, not in the visual axis, but at a considerable angle to it.

Read before the New England Ophthalmological Society, April 18, 1951.

1. (*a*) Schepens, C. L.: Retinal Detachment and Aphakia, Arch. Ophth. **45**:1 (Jan.) 1951. (*b*) Schepens, C. L., and Bahn, G. C.: Examination of the Ora Serrata: Its Importance in Retinal Detachment, ibid. **44**:677 (Nov.) 1950.

2. Jackson, E.: Skiascopy, (The Shadow-Test, Retinoscopy) and Its Practical Application, in Norris, W. F., and Oliver, C. A.: System of Diseases of the Eye, by American, British, Dutch, French, German, and Spanish authors, Philadelphia, J. B. Lippincott Company, 1897, p. 98.

In this connection, it is well known that the peripheral zone of the cornea is irregularly flattened as compared with the central zone and is somewhat thicker.[3] It would appear, consequently, that an irregular astigmatism is present in the oblique axis of the normal eye, owing to aberration in the corneal periphery, and that this is an important factor in producing the blur in the peripheral fundus seen in direct ophthalmoscopy. Another factor operative in producing distortion of the peripheral fundus is the fact that the entering and returning light rays of the ophthalmoscope must pass obliquely through the periphery of the cornea to reach their destination, rather than travel in the optical axis, and a pencil of light falling obliquely on a refracting surface becomes astigmatic. Still a third factor is loss of corneal transparency near the limbus with advancing age, a change particularly noticeable in arcus senilis. If it were possible to have an optical surface which eliminated the peripheral irregular astigmatism of the cornea and was also perpendicular to entering light rays throughout, and if it were further possible to have some prismatic action, so that entering light rays could avoid the partially opaque corneal periphery and then be bent to reach the peripheral fundus, one would logically expect a much clearer view of the periphery of the fundus. This combination of corrected optical factors, with resultant clearer vision, can, in fact, be readily obtained by the use of the contact glass of Troncoso [4] in association with direct ophthalmoscopy.

This plastic lens was first described in 1945 for use in gonioscopy. It has a hemispherical upper part, ending in a peripheral flange, which holds to the sclera around the cornea, so that the lens follows the movement of the eyeball. The lens has practically no astigmatism and gives clear images. A prismatic effect, base toward the center of the cornea, is present in the periphery of the lens. With the patient recumbent, the contact glass is applied over the lightly anesthetized eyeball, and the space over the cornea is filled with saline from a bulb syringe. A preliminary washing of the inner lens surface with a wetting agent and saline prevents air bubbles from adhering to the plastic surface. The ophthalmoscopist moves the light around the eye and is aided by appropriate movements of the patient's head and eyes.

Thirty patients who had easily identifiable choroidal or retinal lesions in the far periphery of the fundus were examined by unaided direct ophthalmoscopy, by direct ophthalmoscopy through the contact glass, and by indirect ophthalmoscopy. The areas which with the ordinary method of direct ophthalmoscopy were blurred, streaked, and indistinct, or else not seen at all, stood out sharply and clearly, for the most part, when the glass was used; in addition, the peripheral field was somewhat wider, though not quite as wide as that seen with the indirect method, with which the images were also strikingly clear-cut (Fig. 1).

With the contact-glass method, one is struck by the great prevalence of degenerative and inflammatory lesions in the fundus periphery, particularly in the elderly.

The contact-glass method was found to be of especial value in the location of retinal tears, particularly the small, and at times multiple, peripheral tears, which

3. Duke-Elder, S. W.: Text-Book of Ophthalmology, Vol. 1, St. Louis, C. V. Mosby Company, 1937, p. 40.

4. Troncoso, M. U.: A New Model of Contact Glass for Gonioscopy (Goniolens), Am. J. Ophth. **28**:1360, 1945.

blend in appearance with the surrounding retina or which at times resemble hemorrhages.[5] Tears of these types may remain unnoticed with the ordinary method of direct ophthalmoscopy, even though the observer's gaze passes over them repeatedly.

A unique situation is present with use of the contact glass in aphakic eyes which have undergone complete iridectomy and show no capsular remnants (Fig. 2). In such eyes, with the direct ophthalmoscope, one may usually observe the retina as far as the ora serrata in the upper one-half of the fundus and, in addition, almost the entire, foreshortened inner aspect of the ciliary body in the region of the coloboma.

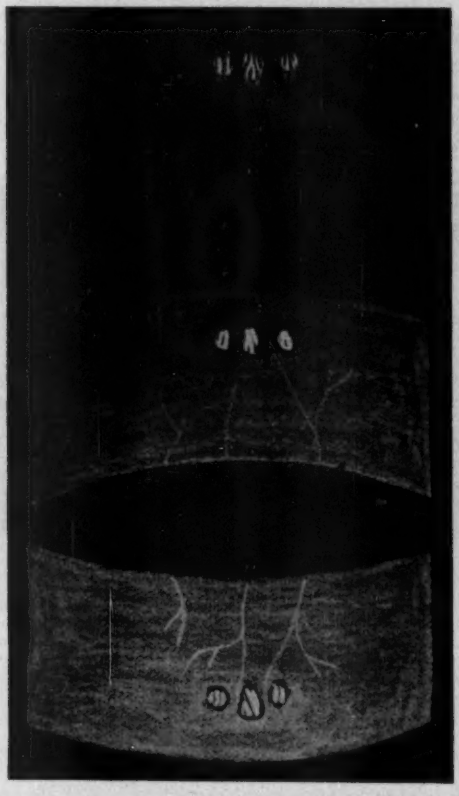

Fig. 1.—Areas of healed choroiditis in the far fundus periphery of the eye of a man aged 74. The upper figure shows the blurred appearance when unaided direct ophthalmoscopy is used. The central figure represents the lesions as seen by direct ophthalmoscopy when the Troncoso contact glass is employed. The lower figure gives the appearance with indirect ophthalmoscopy. A much sharper image is obtained with the last two methods.

5. Arruga, H.: Cirurgia ocular, Ed. 2, Buenos Aires, Salvat Editores, S. A., 1950, p. 587.

USE OF ANTERIOR-SCLERAL TRANSILLUMINATION

When a lighted ophthalmoscope bulb is placed against the anterior sclera, either directly or with the lid tissues intervening, the light travels through the sclera much as it would through plastic, being obstructed mainly by pigment accumulations, and weakening directly with the distance from the source. Consequently, both the exterior and the interior of the globe are illuminated in characteristic patterns, determined mainly by the disposition of uveal pigment.

A. Use for Delineation of Ciliary Body on External Surface of Globe.—The ring of the ciliary body is roughly 6.5 mm. in width, the anterior one-third of which is occupied by the ciliary processes, while the pars plana takes up the posterior two-thirds.[6] The ciliary body is bounded posteriorly by the scalloped, heavily pigmented ora serrata. Slight, dark meridional striae run from the teeth of the ora into the valleys between the ciliary processes.

Fig. 2.—Composite picture of appearance of the peripheral fundus, ciliary body, and chamber angle as seen by direct ophthalmoscopy of the aphakic eye with the contact glass of Troncoso in place. An intracapsular extraction with complete iridectomy had been performed on this eye of a man aged 61. With the pupil dilated, the peripheral fundus up to and including the ora serrata is visible in the upper one-half of the eye. In addition, the foreshortened inner aspect of the ciliary body can be observed in its entirety in the region of the coloboma of the iris.

In this figure, *cd* indicates inner dome of cornea; *t*, sclerocorneal trabeculum; *cbb*, the ciliary-body band; *cp*, ciliary processes; *pp*, pars plana; *c*, cornea; *i*, iris; *bp*, border of pupil; *os*, ora serrata; *fp*, fundus periphery; *trv*, terminal retinal vessel; *bir*, border of irridectomy site.

These structures can frequently be seen in outline by transillumination. The procedure is carried out in a completely darkened room with the observer somewhat dark-adapted. The lighted ophthalmoscope bulb is placed under the lid against the sclera, or against the lightly anesthetized sclera itself, in such a fashion that the light bulb is covered by the surrounding tissues, so that the glare does not distract the observer. The sclera opposite the light is observed (Fig. 3). Posteriorly is seen the dark dentate fringe of the ora serrata. Anterior to this is an illuminated band, indicating the pars plana, often containing dark lines, representing the meridional striae. Still more anterior is another dark band, some 2 mm. in width,

6. Wolff, E.: The Anatomy of the Eye and Orbit, Ed. 2, Philadelphia, The Blakiston Company, 1940, p. 44.

representing the region of the ciliary processes. Most anterior of all is a translucent band, indicating the scleral limbus.

This ciliary body pattern can be seen in the majority of light-complexioned adults and is especially pronounced in the elderly. In children and in heavily pigmented eyes it is much less distinct, appearing only as a poorly defined, uniform dark band. In the Negro, usually the ciliary body cannot be transilluminated.

This type of transillumination is mainly of value in situations not directly associated with ophthalmoscopy. For example, the anterior translucent zone, indicating the scleral limbus, may be of use in indicating the anterior limit of the ciliary body when a scleral incision is made in antiglaucoma operations. The ciliary body pattern may be helpful in cyclodiathermy procedures. The ora serrata shadow may be used to indicate the anterior limit for diathermy in cases of retinal detachment. Light-blocking lesions of the ciliary zone cast dark shadows with this procedure.

Fig. 3.—Ciliary body shadow seen by anterior-scleral transillumination in a light-complexioned man aged 51. Posteriorly is seen the dark dentate fringe of the ora serrata. Anterior to this is an illuminated band, indicating the pars plana. Still more anterior is a second dark band, representing the region of the ciliary processes. Most anterior of all is a translucent band, indicating the scleral limbus. Modified from Duke-Elder[7b] and from Lindahl.[7a]

The procedure may, however, be of some value in ophthalmoscopy by delineating on the external surface of the globe the anterior limit of the retina. This delineation makes possible the localization of retinal lesions by transillumination with the ora serrata as a line of reference, rather than the limbus. In addition, since a small, intense beam of light thrown upon the retina is visible on the exterior of the globe, one can determine the width of the anterior band of retina, ordinarily inaccessible to ophthalmoscopy.

B. Use for Observation of Posterior Fundus.—In this procedure, the direct method of Lindahl,[7] the light bulb is held in contact with the sclera, as in trans-

7. (*a*) Lindahl, C.: Über Durchleuchtungsmethoden zum Nachweis von Chorioidealtumoren, Ztschr. Augenh. **65**:11, 1920. (*b*) Duke-Elder, S. W.: Text-Book of Ophthalmology, Vol. 2, St. Louis, C. V. Mosby Company, 1938, p. 1154.

illumination of the ciliary body; but now the examiner looks directly into the eye, employing, if necessary, an unlighted ophthalmoscope for its correcting lenses. The fundus is dimly illuminated by the light which the scleral tissue has conducted posteriorly. The fundus has a tessellated appearance, with the choroidal vessels showing as a luminous red network, whose interstices are much darker because of the choroidal pigment. The optic nerve appears white. Retinal vessels are usually not distinguishable except at the disk, where they show as dark lines.

Fig. 4.—Ophthalmoscopic transillumination. The upper figure shows a juxtapapillary malignant melanoma as seen by ordinary direct ophthalmoscopy. The lower figure shows the same fundus as that seen by ophthalmoscopic transillumination, in which the light is held as in Figure 3, with the observer looking directly into the eye. The tumor is seen as larger than indicated in the upper figure and has a serrated border. The figures are from the right eye of a white man aged 49, who had noticed somewhat blurred vision in that eye for one year. Vision was 20/30 +2 in the right eye and 20/15 in the left eye. Pathologic examination showed the tumor extending to the degree indicated in the lower figure. The melanoma was moderately pigmented and was composed of spindle cells in a vascularized matrix.

A variety of pathologic fundus conditions can be observed to advantage with this method. Serous detachment of the retina appears as an area of luminous red,[7a]

instead of the opaque gray noted with ordinary ophthalmoscopy. Pigmented tumors are dark, and the transillumination may at times reveal flat extensions of these tumors not otherwise visible (Fig. 4). Even small pigmented tumors, such as those involving merely the central macular area, usually stand out clearly. A pigmented tumor beneath a detachment is dark, whereas any detached retina beyond the tumor is red.[7a] Consequently, the differential diagnosis of simple detachment and detachment complicated by tumor [8] is especially aided by this method.[9] Blood generally gives a dull red glow with this procedure. An area of fresh choroiditis shows white. The dense pigment ring about old choroidal inflammatory lesions shows up sharply; in addition, the central portion of the lesion may appear as an irregular mass with intermingled white and dark areas. A benign nevus appears as a flat, black patch on the red background. Pigment-free tumors are usually translucent.

It is important to remember in transillumination that pigmentation does not necessarily accompany malignant growth, so that in both primary and metastatic tumors pigment content varies from absence to heavy concentration.[10] It should

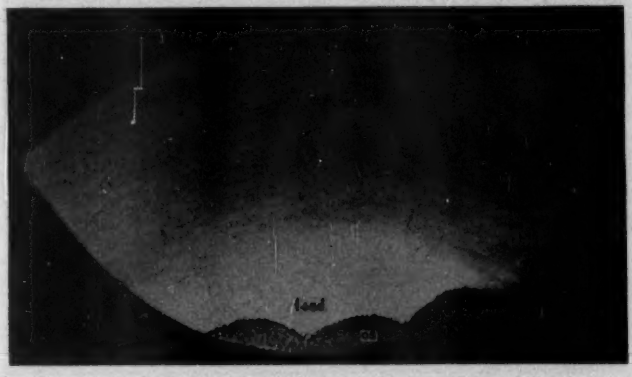

Fig. 5.—View of the fundus periphery of a normal eye, with crystalline lens in situ, of a dark-complexioned man aged 37, as seen with indirect ophthalmoscopic transillumination. The observer wears a +3.00 D. accommodative lens, held in a light trial frame, before his dominant eye. One hand holds the light, as shown in Figure 3, with the sclera slightly indented. The other hand holds a +20.00 D. lens before the subject's eye to form the real, inverted fundus image. The brilliantly illuminated mound is the site where the ophthalmoscope bulb presses on the scleral surface, seen from the fundus side. Below, the dark, granular ora serrata is visible. Not shown are the branching terminals of the retinal vessels ending near the ora, and the straight, parallel peripheral choroidal vessels disappearing beneath the ora.

Here, *os* indicates the ora serrata; *l+sd*, the combined light source and scleral depressor.

also be noted that certain benign lesions, such as tumors, old inflammatory masses, and, particularly, old blood collections, may be light-obstructing.[9]

C. Use for Observation of Anterior Fundus.—The observations noted with reference to direct ophthalmoscopic transillumination of the posterior fundus hold true for the anterior portion as well. The far periphery, however, appears blurred,

8. (*a*) Duke-Elder, S. W.: Text-Book of Ophthalmology, Vol. 3, St. Louis, C. V. Mosby Company, 1941, p. 2483. (*b*) Samuels, B.: Detachment of the Retina in Early Sarcoma (Malignant Melanoma) of the Choroid, Arch. Ophth. **42**:620 (Nov.) 1949.

9. Duke-Elder,[8a] pp. 2514, 2908.

10. Duke-Elder,[8a] p. 2462.

despite the brilliance of the light source, now almost directly in the observer's line of vision. The intensity of the light at the periphery, however, can be utilized to convert the indistinct direct image into a clear indirect one, as in indirect ophthalmoscopy. The observer wears a + 3.00 D. accommodative lens, set in a light trial frame, before his dominant eye. One hand controls the light source by means of the handle of a small ophthalmoscope whose bulb is placed in contact with the sclera, either directly or through the lid, in the region of the ora serrata. The other hand holds a + 20.00 D. condensing lens, which forms the real, inverted fundus image. A strikingly clear image of the peripheral fundus is obtained. In addition, when slight pressure with the ophthalmoscope bulb is made upon the sclera, the most peripherally situated structures, i. e., the ora serrata and, at times, part of the pars plana, are brought into the line of observation. In this way, with the observer following the light, which he moves around the circumference of the globe, the

Fig. 6.—Example of fundus detail which can be seen by transillumination with indirect ophthalmoscopy. Below are three cystic areas of retinal degeneration at the fundus periphery. Central to these is an area of healed choroiditis. At the lower left is seen the brilliant mound of the ophthalmoscope bulb, which has pressed the ora serrata into the observer's line of vision. The picture is from the right eye of a man aged 52 who showed numerous similar areas throughout the fundus periphery of both eyes. One year prior to examination the patient had had a traumatic rupture of the choroid and macular hemorrhage in the right eye. No detachment was present. The Wassermann reaction of the blood was negative. Pronounced pyorrhea alveolaris had been present at least 10 years.

Here, *l* indicates the light source; *os*, ora serrata; *rdg*, areas of retinal degeneration; *ch*, healed choroiditis.

entire region of the ora serrata can be examined in most eyes (Fig. 5). A great amount of detail is seen in the vicinity of the light source. The granular, darkly pigmented ora serrata stands out sharply. The pars plana appears orange, and its darker meridional striae are seen coming from the teeth of the ora. The branching terminals of the retinal vessels are seen as they approach the pigment fringe. The straight, parallel choroidal vessels at the periphery are observed disappearing beneath the ora serrata. Many fine retinal changes in the fundus periphery can be well seen with this method. Pigment changes, degenerative areas, and cysts in the retina usually stand out clearly (Fig. 6). Small retinal breaks in serous detachment

often are strikingly distinct owing to the illuminated choroid shining through the retinal defect. Choroidal changes are especially distinct because of the associated pigment disturbance; but should they underlie retinal breaks, detection of the latter is seriously interfered with because of the confusing combined picture. In such instances ordinary indirect ophthalmoscopy gives by far the better picture. The transillumination method just described is especially useful in the detection of light-blocking lesions, for which purpose it can be used even in heavily pigmented eyes.

Fig. 7.—Headlight which may be employed as an electric ophthalmoscope in the indirect method. It can be used attached to the head band or detached and held in the hand.

USE OF SIMPLE TYPE, ELECTRIC INDIRECT OPHTHALMOSCOPE

Almost all observers who use the direct and indirect methods of ophthalmoscopy believe that the indirect method is preferable [11] in examining the periphery of the fundus, for it gives a wider field and a clearer image. Its use, however, has been handicapped by the lack of suitable, self-illuminating electrical instruments.

There is commercially available, however, an electric instrument (Fig. 7) which may be used as a satisfactory ophthalmoscope in the indirect method—the National Electric Instrument Company's "Center of Beam" headlight.[12] This light is com-

11. Schepens.[1a] Arruga, H.: The Relative Importance of Direct and Indirect Ophthalmoscopic Examination in the Treatment of Retinal Detachment, Brit. J. Ophth. **33**:651, 1949.

12. National Electric Instrument Company, Inc., 92-21 Corona Ave., Elmhurst, N. Y.

posed of a base, a condensing lens, and a mirror. At one end of the base is the cord, whose terminals fit any simple type of rheostat; at the other end is the lamp, around which prongs extend. A metal tube holding the condensing lens slides over the prongs. Over the condensing lens is placed a centrally perforated mirror, at such an angle that the observer's visual axis is in line with the emerging light beam—the basic requirement for an ophthalmoscope. A + 3.00 D. lens for accommodation is held behind the mirror by a thin metal band or in a trial frame before the observer's eye. The light is adjusted so that the emerging beam is focused at 0.33 + meter, the focus being an image of the bulb filament. A + 20.00 D. lens is held before the patient's eye to form the real, inverted fundus image. A rather small, but brilliantly illuminated, area of the fundus is seen.

A similar ophthalmoscope was recently constructed and described by Epstein,[13] who later found it to be commercially available. He used it reversed and wore it attached to a head band during operations for retinal detachment and for the removal under direct vision of intraocular Cysticercus and foreign bodies. The instrument was employed both for direct and for indirect ophthalmoscopy. Worn attached to the head band, the instrument may be conveniently used in indirect ophthalmoscopy to allow one hand to be free for the maneuver of scleral compression [14] in bringing the region of the ora serrata into view. If the ophthalmoscope light bulb is used as a scleral depressor, one has the advantage of being able alternately to switch on and off the transilluminating light and thus obtain contrasting views.

SUMMARY

It is suggested that aberration at the periphery of the cornea is an important factor in the peripheral fundus blur noted in direct ophthalmoscopy.

The contact glass of Troncoso has been found useful in direct ophthalmoscopy by clarifying the peripheral-fundus image.

The ciliary body shadow can often be seen in great detail on the external surface of the globe when anterior-scleral transillumination is used.

The advantages of direct ophthalmoscopic transillumination for examination of the posterior fundus are noted.

A method of transillumination with indirect ophthalmoscopy for observation of the anterior fundus is described.

A simple-type, commercially available headlight may be usefully employed as an electric ophthalmoscope in the indirect method.

355 Thayer St. (6).

13. Epstein, E.: An Ophthalmoscope for Use in Operations, Arch. Ophth. **43**:373 (Feb.) 1950.

14. Schepens.[13] Trantas, A.: Moyens d'explorer par l'ophtalmoscope, et par la translucidité; la partie antérieure du fond oculaire, le cercle ciliaire y compris, Arch. opht. **20**:314, 1900.

CLINICAL AND AUTOPSY FINDINGS IN EARLY RETROLENTAL FIBROPLASIA

Report of a Case

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AND
WILLIAM C. FRAYER, M.D.
PHILADELPHIA

FEW REPORTS of the pathologic changes in early cases of retrolental fibroplasia have appeared in the literature. Heath,[1] in 1950, classified retrolental fibroplasia as a syndrome and described the pathologic findings in the early and later stages of retrolental fibroplasia in premature infants. He described the primary disease as "an edematous, hemorrhagic and proliferative process associated with hamartomatous neovascular tissue in the retina, a process best described as a retinopathy of premature birth." Heath defined "hamartoma" as an accumulation of vascular tissue, normal in location but excessive in amount, and without the property of malignant growth.

Reese,[2] in 1951, described the autopsy observations in a case of early retrolental fibroplasia. Sections of these eyes showed "angiomatous tissue extending from the retina into the vitreous, particularly in the periphery around the base of the vitreous." Reese stated that the outstanding feature is the angioplastic process in the vitreous and that the disease is primarily one of the vitreous, the retina participating in the process only as a source of newly formed vessels.

Friedenwald, Owens, and Owens,[3] in a paper discussed by Heath and Reese, presented their observations on the early pathologic changes arising in retrolental fibroplasia. There seems to be agreement that in the early stage of retrolental fibroplasia in premature infants the primary pathologic change is an exudative phase, characterized by the presence of edema and proliferation of blood vessels confined to the inner layers of the peripheral retina, followed by, or associated with, changes in the vitreous, which result in organization and fibrosis.

It seems of some value, therefore, to present another pathologic report of the ocular changes seen in an early case of retrolental fibroplasia. The clinical findings in this case, and our first experience with corticotropin (ACTH) in this disease,

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From the Departments of Ophthalmology and Pathology, Hospital of the University of Pennsylvania and the Children's Hospital of Philadelphia.

1. Heath, P.: Retrolental Fibroplasia as a Syndrome: Pathogenesis and Classifications, Arch. Ophth. **44**:245-274 (Aug.) 1950.

2. Reese, A. B., and Blodi, F. C.: Retrolental Fibroplasia, Am. J. Ophth. **34**:1-24 (Jan.) 1951.

3. Friedenwald, J. S.; Owens, W. C., and Owens, E. U.: Read at the Eighty-Seventh Annual Meeting of the American Ophthalmological Society, June 7-9, 1951, White Sulphur Springs, W. Va., to be published.

were originally presented before the Section on Ophthalmology of the College of Physicians of Philadelphia on March 16, 1950, in a discussion on a paper on retrolental fibroplasia by Dr. Algernon Reese. They later appeared in the ARCHIVES.[4]

REPORT OF CASE

L. L., a premature Negro girl, was born on Nov. 7, 1949, with a weight of 905 gm. She was the first of twins delivered after a gestation of 22 or 23 weeks. The sibling survived only a few hours. The only known causes of prematurity were the twin gestation and premature rupture of the membranes. The eyes of the patient were first examined on the 53d day after birth. Initial examination of the right eye showed a persistent anterior pupillary membrane and extremely dilated and tortuous veins. The condition of the left eye was essentially the same except that along the course of the superior temporal vessels was a well-defined area which was thought to be a hemorrhage or an aneurysmal dilatation. Subsequent ophthalmoscopic examinations revealed retinal detachment in the periphery of each eye.

On the 61st day after birth a clinical diagnosis of retrolental fibroplasia was made. Although corticotropin had not been used in this disease to our knowledge, a course of treatment with the drug was instituted, at the suggestion of Dr. Joseph Stokes, chief of the pediatric clinic of the Hospital of the University of Pennsylvania, and physician-in-charge of Children's Hospital of Philadelphia.

The patient was treated with 5 mg. of corticotropin every six hours, for a total of 263 mg., given over a period of 14 days. During the course of treatment with the drug, a pustular eruption of the skin, some rounding of the facial contours, and prominence of the globes developed. At the time of death, at the age of 3½ months, she showed generalized exfoliative dermatitis. Ophthalmoscopic examination four days before death showed only cicatricial changes in the periphery of the retina of each eye and a "congenital retinal fold" in the right eye. The acute inflammatory signs appeared ophthalmoscopically to have completely subsided. The area of retinal involvement in each eye corresponded to that seen at the time of the institution of corticotropin therapy. Despite the lack of definite evidence that corticotropin treatment had altered the course of the disease, the areas of involvement did not increase after the therapy was instituted. It was believed that this drug may have been a contributing factor in the death of the child.

Autopsy.—A general postmortem examination revealed that the significant changes were confined to the eyes, skin, and peritoneal cavity. A generalized exfoliative dermatitis was found, and histologic examination of sections of the skin revealed a nonspecific reaction, compatible with Leiner's disease (desquamative erythroderma). Diffuse, mild, acute peritonitis was also present. The adrenal glands were normal except for mild acute inflammation of the periglandular tissues.

Pathologic Examination of Eyes.—Both eyes were enucleated shortly after birth. They were embedded in pyroxylin, sectioned, and stained with hematoxylin and eosin. Except for minor variations, the findings were similar in the two eyes.

Gross Description: Each eye measured 17 by 16 by 16 mm. The corneas were clear. The anterior chambers were of normal depth. Transillumination showed nothing abnormal. Horizontal section revealed white proliferative or exudative material over the ciliary body.

Microscopic Description[5]: Cornea: The cornea appeared entirely normal.

Anterior chamber: The chamber was of normal depth and contained a few scattered round cells, which lined the cavity and the trabecular spaces.

Iris: The iris stroma contained an excessive number of thin-walled vascular channels (Fig. 1).

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4. Scheie, H. G.; Tyner, G. S.; Buessler, J. A., and Alfano, J. E.: Adrenocorticotropic Hormone (ACTH) and Cortisone in Ophthalmology, A. M. A. Arch. Ophth. **45**:301-316 (March) 1951.

5. The findings were similar in the two eyes. Figures 1 to 6, from sections of the left eye, were used because the photographs were the clearest. Figures 7 and 8 are of the right eye.

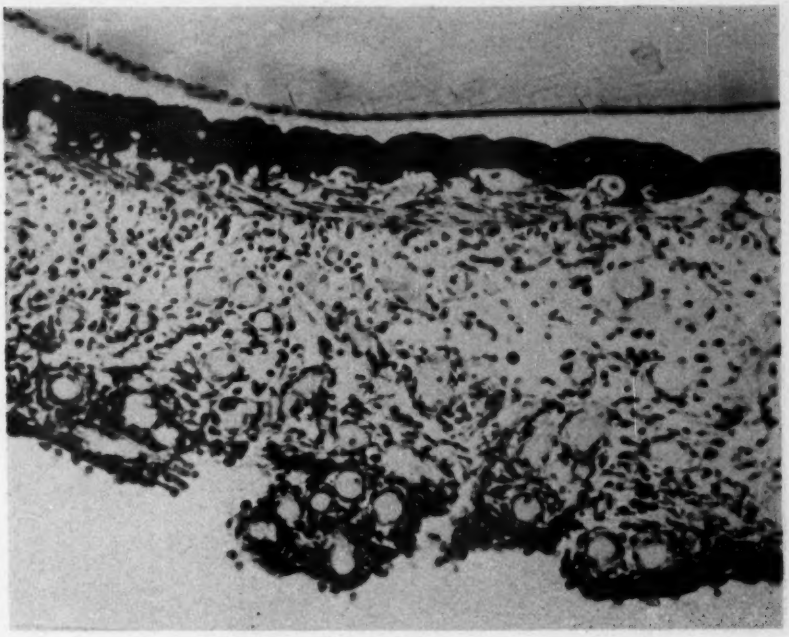

Fig. 1.—Iris of the left eye, showing extensive vascularization of the stroma. × 230.

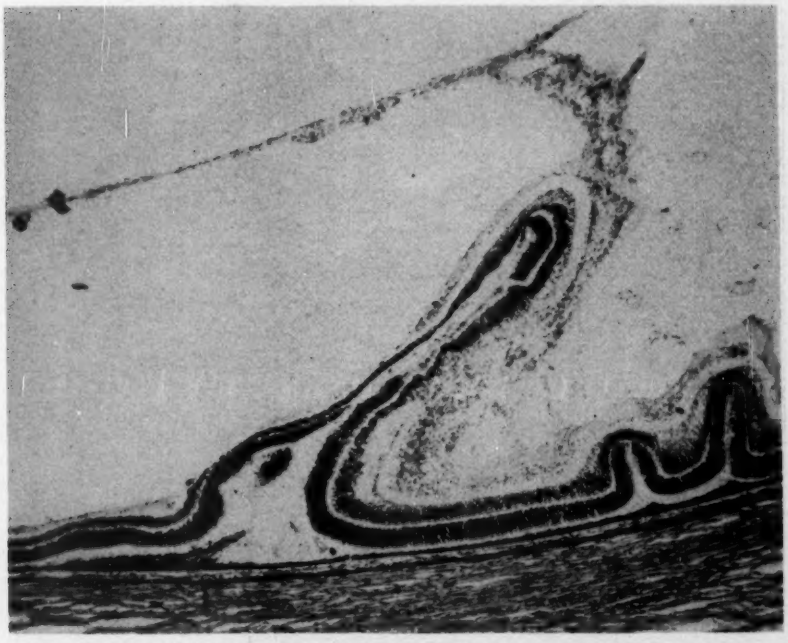

Fig. 2.—Retinal fold in the left eye. Note proliferation of pigment epithelium beneath the fold and early fibrovascular membrane at the apex. × 54.

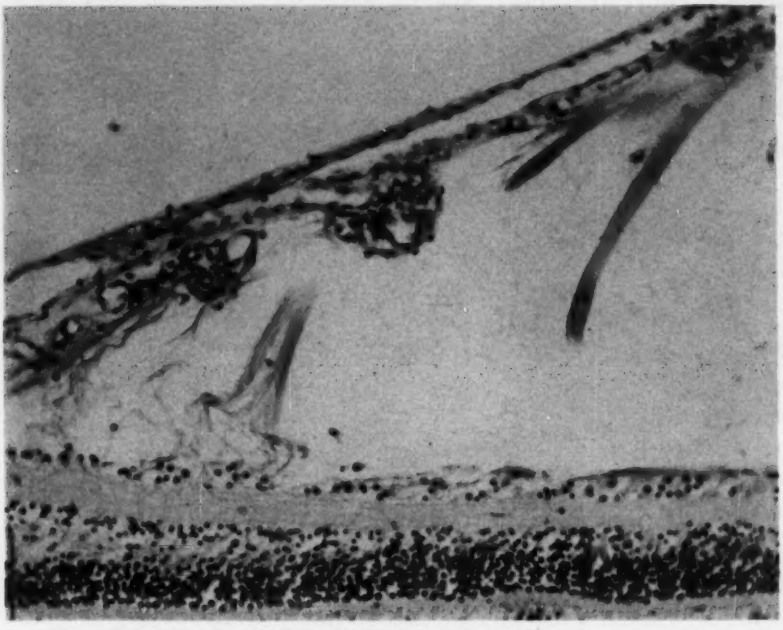

Fig. 3.—Higher magnification of the vascular membrane as it arises from the retina posterior to the fold in the left eye. × 195.

Fig. 4.—Vascular buds arising from the nerve fiber layer at the apex of the retinal fold. × 540.

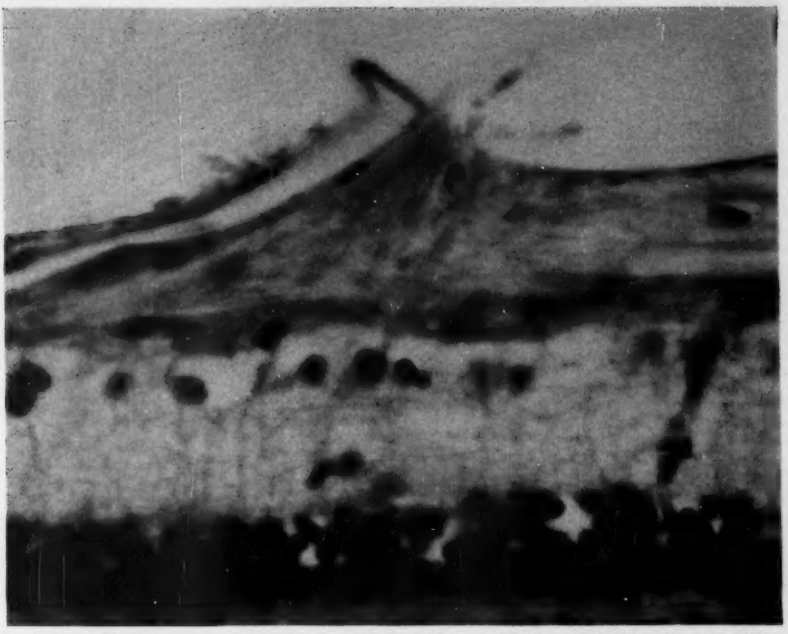

Fig. 5.—Small vascular bud near the optic papilla, representing the origin of a new fibrovascular membrane. × 650.

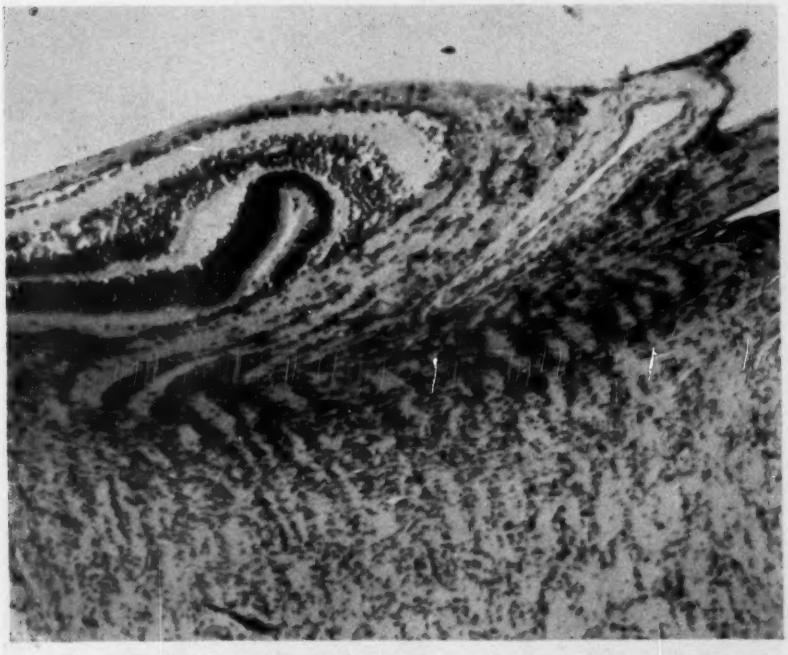

Fig. 6.—Fold of the retina overlying the optic papilla in the left eye. × 110.

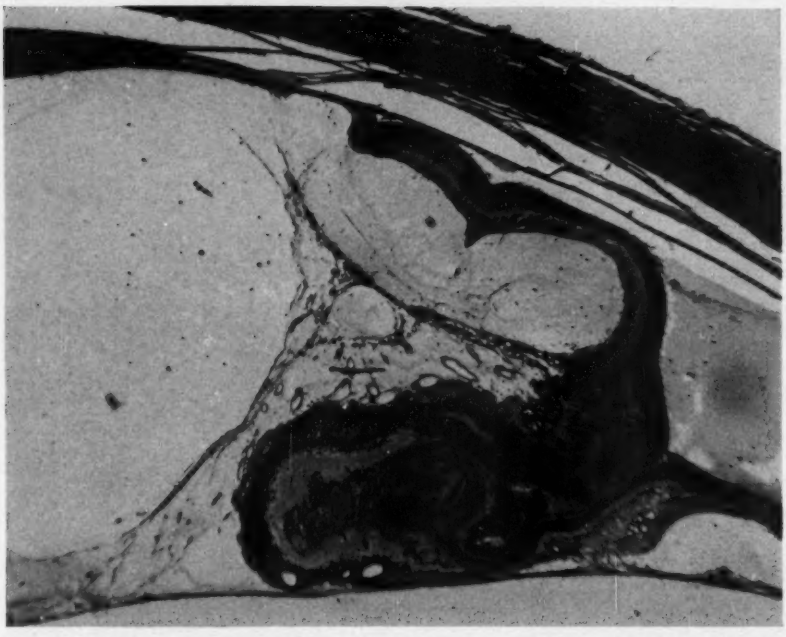

Fig. 7.—Retinal fold at the ora serrata of the right eye. Note vascular tissue within the retina at the apex. × 34.

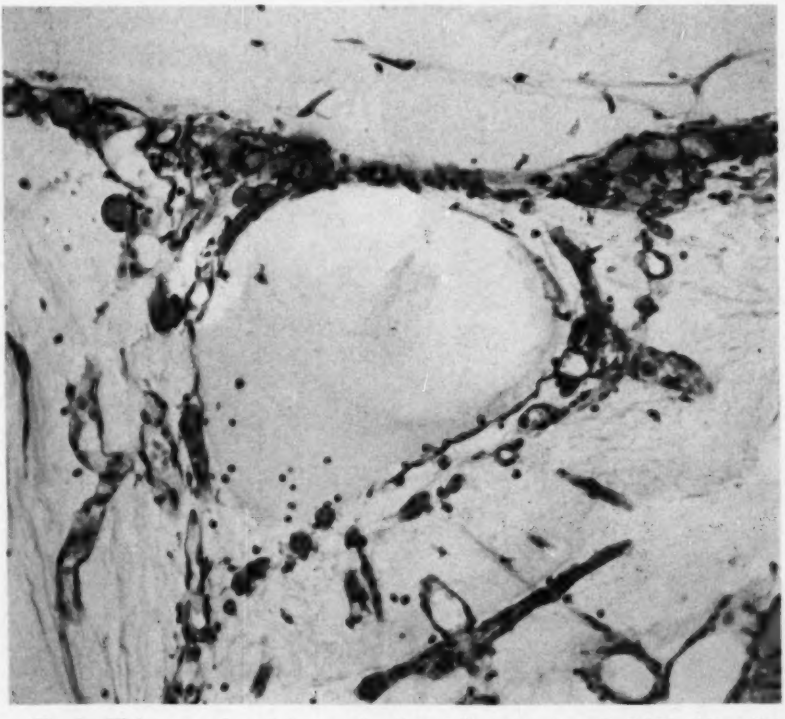

Fig. 8.—High power view of the vascular tissue adjacent to the retinal fold of the right eye. × 200.

Ciliary body: The ciliary musculature was normal. The vessels of the ciliary processes were intensely congested.

Choroid: The choroid was normal.

Retina: Arising from the retina in the region of the ora serrata was a heavily vascularized fibrous membrane directed toward the posterior surface of the lens, representing an early stage of organization and fibrosis within the vitreous (Figs. 2 and 3). Contraction of this membrane appeared to be pulling an irregular fold of retina away from its bed on the pigment epithelium and toward the central portion of the globe. The vascularity of the membrane surrounding this fold of retina was particularly pronounced anteriorly, where innumerable small, thin-walled vessels were observed within a loose fibrillar network. This excessive vascularity demonstrates the hamartomatous character of the process. Small hemorrhages were apparent adjacent to some of these tortuous new vessels. This vascular tissue arose entirely from the innermost layers of the retina, sending small vascular buds into the vitreous (Figs. 4 and 5). Numerous smaller membranes arose from the retina near the optic papilla and swept forward to join the larger membrane in its course toward the posterior surface of the lens.

Beneath the large fold of retina in the region of the ora serrata, the subretinal space was filled with edema fluid, and there were large vacuoles within the retina. These changes are consistent with Heath's thesis that the retrolental fibroplasia of prematurity is, in part, an edematous process within the retina.

A second retinal fold was drawn over the optic papilla from the temporal side (Fig. 6) of the left eye. From its apex, a thin fibrovascular membrane could be followed through the vitreous for a short distance. A small amount of edema fluid was present beneath this fold. The pigment epithelium showed disorganization and proliferation beneath both retinal folds. Figures 7 and 8, from the right eye, show views of the retinal fold and adjacent vascular tissue.

Optic nerve: The optic nerve was entirely normal.

Sclera: The sclera showed no histologic lesions.

SUMMARY

A clinical and pathologic report is presented on both eyes of a premature infant with bilateral retrolental fibroplasia in its early stages. This infant was treated with corticotropin as soon as a definite diagnosis was established. Five milligrams of corticotropin was given every six hours over a period of 14 days. During the last few days the dose was tapered off, the patient receiving a total of 263 mg. During the course of treatment a generalized pustular eruption of the skin, some rounding of the facial contours, and prominence of the globes developed. At the time of death the child showed a generalized exfoliative dermatitis. The principal changes seen at autopsy were confined to the eyes, skin, and peritoneal cavity. The cause of death was thought to be acute peritonitis. It is believed that corticotropin therapy may have contributed to the death of the child. Evaluation of the effect of corticotropin on this disease cannot be made on the basis of a single case, but it was our feeling that the areas of retinal involvement did not increase after treatment with the drug.

The principal pathologic changes seen in microscopic examination of the eyes were as follows:

1. A heavily vascularized fibrous membrane, arising from the inner layers of the retina and pulling a retinal fold forward from the region of the ora serrata toward the central portion of the globe.

2. Small vascular buds arising from the vessels in the nerve fiber layer of the retina and extending into the vitreous.

3. Formation of retinal folds, arising from the surface of the retina near the optic papilla and joined by fibrovascular bands to a larger retinal fold in the periphery of the retina, which extended outward toward the central portion of the globe.

4. Presence of edema fluid and small areas of proliferation of pigment epithelium of the retina.

5. Excessive small, blood-filled vascular channels in the iris and ciliary body.

CONCLUSIONS

As reported by Heath, Reese, Friedenwald, and others, the outstanding histologic change in early retrolental fibroplasia occurring in premature infants appears to be an angioplastic process, occurring mainly in the periphery of the retina and involving only the inner layers of the retina. The proliferative vascular tissue is supplied by the vessels of the retina, and the proliferation is followed by, or associated with, changes in the vitreous, which result in organization and fibrosis. In this case the eyes showed similar changes.

VARIABLE OPHTHALMOPLEGIA DUE TO ANGIONEUROTIC EDEMA

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AND
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ALLERGIC ocular manifestations have been the subject of considerable interest on the part of ophthalmologists in recent years. Excellent reviews have been made by Appelbaum,[1] Lemoine,[2] Duggan,[3] and the Leopolds.[4] A survey of the literature indicates that nearly all the structures of the eye are potential sites of allergic reactions. When various allergic manifestations referable to the eye are mentioned, angioneurotic edema is included regularly but is usually considered as a process limited to the eyelids so far as the eye is concerned. Occasionally reference has been made to more widespread ocular involvement on the basis of angioneurotic edema. The appearance of ophthalmoplegia as the most prominent ocular manifestation of angioneurotic edema would appear to be extremely rare. Therefore, the following case is deemed worthy of presentation as a striking example of variable ophthalmoplegia due to angioneurotic edema.

REPORT OF A CASE

History.—M. H., a married white woman aged 25, was first examined in the outpatient department on Dec. 7, 1949, and subsequently admitted to the Wills Hospital on March 1, 1950, in the service of one of us (W. E. F.). The father was subject to hay fever, and the mother and a brother had a history of urticaria, the mother showing this reaction to milk.

The past medical history revealed that the patient had been subject to frequent headaches since childhood. A generalized convulsive seizure had occurred on one occasion, at the age of 2 years. A copper-colored macular skin eruption had been present over the arms and legs at about 5 years of age but had not recurred subsequently. There had been frequent sore throats and occasional attacks of quinsy (peritonsillar abscess) until 1943, when tonsillectomy was performed.

Immediately after the tonsillectomy frontal headaches of great severity developed. Several months later double vision on right lateral gaze was first observed. This diplopia continued intermittently, and two years later the patient started to experience episodic swelling of the eyelids and periorbital facial tissues, variably affecting the eyes but usually the right eye. In

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From the Wills Hospital.

Read before the College of Physicians of Philadelphia, Section on Ophthalmology, Dec. 21, 1950.

1. Appelbaum, A.: Allergic Phenomena in Ophthalmology, Arch. Ophth. **24**:803 (Oct.) 1940.

2. Lemoine, A. N.: Allergies in Ophthalmology, Arch. Ophth. **28**:79 (July) 1942.

3. Duggan, W. F.: Vascular Basis of Allergy of the Eye and Its Adnexa, Arch. Ophth. **36**:551 (Nov.) 1946.

4. Leopold, I. H., and Leopold, H. C.: Allergy in Ophthalmology, Tr. Pennsylvania Acad. Ophth. & Otolaryng. May, 1950, pp. 13-47.

these episodes, the edema would develop rapidly overnight and would be associated with prominent drooping of the swollen eyelid and unpredictable deviation of the involved eye in various directions, as well as aching pain in the forehead and nose on the affected side and vomiting at times. The swelling and pain would subside within 24 or 48 hours, but the drooping of the eyelid would persist for as long as one or two weeks, and during this period the ocular deviation would often shift from one direction to another. These episodes recurred on the average of once or twice a month, with no temporal relation to the menses. During the past year ocular deviation and diplopia had been present more or less constantly, the deviation of the affected eye often changing its direction during the night. Various forms of medication, including use of antihistaminics, had afforded no relief. Noteworthy was the fact that when the patient temporarily ceased her work as a textile mill employee and moved to a neighboring state there was a remission of symptoms, with subsequent exacerbation upon return to her home and job.

Examination.—The patient was well developed, and her appearance corresponded with her chronological age. The heart, lungs, and abdomen were grossly normal. The blood pressure was 110/72.

Neurological examination revealed the station and gait to be within normal limits. Motor power, coordination, reflexes, and sensation were intact over the trunk and in the extremities. The fundus was within normal limits bilaterally, with the media clear, the disk margins distinct, the disk color normal, and the vessels normal. The visual acuity was 6/6—2 in the right eye and 6/6 in the left eye. Perimetric examination of the visual fields showed no peripheral or central defect. There was no exophthalmos. The pupils were equal and regular and reacted well to light and in accommodation. There was no ocular deviation with the eyes in the primary position, but there was limitation of external gaze bilaterally, with some limitation of inward gaze with the right eye. The corneal reflexes were equally active, and there was no disturbance of sensation over the face. No facial, palatal, or lingual weakness was observed.

Laboratory Data.—The urine was normal. Blood studies revealed 13 gm. of hemoglobin per 100 cc., 4,300,000 red cells, and 6,500 white cells, with 72% neutrophils, 20% lymphocytes, 5% monocytes, 2% eosinophils, and 1% basophils. The Wassermann and Kahn reactions of the blood were negative. The blood sugar measured 83 mg. per 100 cc. The cerebrospinal fluid was clear and colorless, with an initial pressure of 120 mm., 1 cell per cubic millimeter, a total protein content of 51 mg. per 100 cc., a negative Wassermann reaction, and a colloidal gold curve of 0000000000. The roentgenogram of the skull showed no evidence of disease in the skull, sella turcica, sinuses, or orbits.

Course.—Repeated examinations of the patient at variable intervals verified the impression that there was marked, unpredictable alteration in her abnormal neuro-ophthalmological findings. On Jan. 18, 1950, there were partial ptosis of the left eyelid and limitation of external gaze bilaterally, as well as limitation of upward gaze with the left eye. Three days later, on January 21, there were marked edema of the right eyelid and almost complete ptosis of the right lid, with deviation of the right eye downward and inward. During the next three days, the edema subsided but the ptosis of the right lid persisted, and it was noted that when the left eye was covered the right eye could be brought back to the primary position from the deviated position downward and inward. As the edema subsided, the skin of the right eyelid appeared brawny and desquamating. On January 26 the right eye was still conspicuously deviated downward (Fig. 1); it could not be turned upward at all, either nasally or temporally. Diplopia was present and was increased upon upward gaze and upon right lateral gaze. Slight limitation of inward gaze of the left eye was present. On January 28 there was another acute exacerbation of edema in the region of the right eye and the ocular deviation changed, so that the right eye was fixed in a slightly downward and outward position (Fig. 2). On the following day, there was less edema, but the ptosis persisted and the ocular deviation had changed to an inward and downward position. On January 30, the edema had completely subsided, and there was only a slight ptosis of the right eyelid, with slight lateral deviation of the right eye. On the following day, January 31, there was no evidence of edema and no ptosis, with no deviation of the right eye in the neutral position but with some limitation of inward, outward, and upward gaze, although no limitation of downward gaze. Slight limitation of outward gaze with the left eye was also present. On February 2 there were some palpebral edema and slight ptosis of the left

eye, with upward and outward deviation of the right eye (Fig. 3). During the interval of approximately one month until her next examination, the patient experienced an episode of slight edema of the right eyelid, accompanied with deviation of the right eye downward and inward, which subsided within a week. Another episode developed on February 26 with initial involvement of the left eye by edema and ptosis, but within 48 hours the condition had spread to involve

Fig. 1.—Pronounced inferior deviation of the right eye on Jan. 26, 1950.

Fig. 2.—Palpebral edema and pronounced ptosis of the right eye on Jan. 28, 1950.

Fig. 3.—Slight ptosis and palpebral edema of the left eye and external deviation of the right eye on Feb. 2, 1950.

the right eye similarly. When she was reexamined on March 1, 1950, there were edema of both eyelids and pronounced ptosis bilaterally, with almost complete inability to move the right eye horizontally, limitation of upward and downward gaze with the right eye, and marked limitation of outward gaze with the left eye. Ten days later, on March 10, there was almost complete subsidence of the edema with evident ptosis of the left eyelid. There were limitation of outward gaze and marked limitation of upward gaze of the left eye; the right eye could be moved

outward fully, but there was inability to move the right eye inward and downward, as well as pronounced limitation of upward gaze (Fig. 4). One week later the right eye was observed to be deviated and fixed in a downward and outward position (Fig. 5).

The patient was investigated for evidence of sensitivity by the scratch and intracutaneous methods. The examiner was skeptical as to whether the elimination and the avoidance of reacting proteins would afford relief. Nevertheless, a diet was recommended on the basis of this study, and the patient was advised to avoid reacting inhalants as much as possible. Since she manifested a rather strong immediate reaction to histamine and Staphylococcus toxoid, as well as a delayed reaction to the latter, a course of hyposensitization with Staphylococcus toxoid, as well as an attempt to build up tolerance to histamine, was arranged. Since the patient soon became pregnant, it was not possible to maintain direct supervision and observation from an

Fig. 4.—Moderate ptosis of the left eye and pronounced limitation of inward gaze of the right eye on March 10, 1950.

Fig. 5.—Pronounced inferior and lateral deviation of the right eye on March 18, 1950.

allergic standpoint. However, the patient reported by letter that during the next few months the condition of her eyes had improved slightly, with this improvement reflected chiefly in diminished swelling and drooping of the eyelids. The patient stated, "My right eyeball still changes position every time there is any swelling and sometimes without any visible swelling. The change in position with or without swelling always occurs overnight." Another noteworthy observation of this patient was expressed as follows: "I can connect swelling and great changes in the position of the right eyeball as being caused by going into a place which has been freshly painted or sprayed with DDT or where other such substances have been used. Even though I leave immediately, it seems that just contact with the air in the place is enough to cause the trouble." This information indicates that the variable, unpredictable edema and ocular deviation have continued to manifest themselves, although possibly diminished in severity during the course of pregnancy. It is expected that intensive direct observation will be resumed after the termination of the pregnancy.

COMMENT

Angioneurotic edema has been a well known clinical syndrome since its description by Quincke.[5] It is characterized by the paroxysmal occurrence of sharply circumscribed, nonpitting edema, involving usually the skin and subcutaneous tissue and sometimes the mucous membranes. It may appear on the face, with the eyelids a common location, and may involve the lips or cheek. The swelling is relatively short in duration, lasting a few hours, or possibly a day or two days, but the edematous area tends to recur often, affecting the same area repeatedly.

A hereditary type undoubtedly occurs in some instances. Asthma, urticaria, and other allergic manifestations may be discovered in the personal and family histories of the patient. The specific allergens in angioneurotic edema, as in urticaria, are likely to be infections, foods, and drugs. Psychogenic and endocrine factors may be of contributing etiologic significance in some cases. According to Cooke,[6] in not over 50% of cases is the cause definitely determined, and delayed reactions to specific allergens are said to be commoner than acute reactions.

Involvement of the nervous system centrally and peripherally as a consequence of angioneurotic edema has been well recognized. Circumscribed edema of the brain was emphasized by Kennedy [7] as a basis for sudden increase of intracranial pressure with papilledema, combined in some instances with clinical evidence of a focal cerebral lesion. Optic neuritis during serum sickness was observed by Mason.[8] Barkan [9] described a case in which angioneurotic edema of the face and eyelids was associated with glaucoma and crises of ocular hypertension; these ocular manifestations disappeared when the angioneurotic edema subsided. Weekers and Barac [10] stated that orbital involvement is an exceptional ocular feature of angioneurotic edema, as compared with the relatively common involvement of the eyelids. Orbital involvement was described by Cassirer and Hirschfeld [11] in the form of temporary and recurrent exophthalmos, alternating as to the side of involvement, with occurrence in patients who had angioneurotic edema of other parts of the body. Ford [12] described a case in which angioneurotic edema of the orbit developed suddenly and produced papilledema, amaurosis, and complete ophthalmoplegia, with rapid subsidence. A case which resembles most closely the one reported here was described in detail by Schroeder, Grana, and Vaghi Mosquera.[13] Their patient, a 14-year-old

5. Quincke, H.: Über akutes umschriebenes Hautoedem, Monatsschr. prakt. Dermat. **1**:129, 1882.

6. Cooke, R. A.: Allergy in Theory and Practice, Philadelphia, W. B. Saunders Company, 1947, pp. 311-314.

7. Kennedy, F.: Cerebral Symptoms Induced by Angioneurotic Edema, Arch. Neurol. & Psychiat. **15**:28 (Jan.) 1926.

8. Mason, V. R.: Optic Neuritis in Serum Sickness, J. A. M. A. **78**:88 (Jan. 14) 1922.

9. Barkan, H.: Ocular Angioneurotic Edema and Glaucoma, Am. J. Ophth. **2**:800, 1919.

10. Weekers, L., and Barac, G.: Les manifestations oculaires de l'œdème de Quincke: L'œdème allergique paroxystique du globe oculaire, Arch. opht. **1**:193, 1937.

11. Cassirer, R., and Hirschfeld, R.: Das akute umschriebene Oedem, in Bumke, O., and Foerster, O.: Handbuch der Neurologie, Vol. 17: Spezielle Neurologie, Berlin, Julius Springer, 1935, pp. 366-400.

12. Ford, F. R.: Diseases of the Nervous System in Infancy, Childhood and Adolescence, Springfield, Ill., Charles C Thomas, Publisher, 1944, p. 1084.

13. Schroeder, A. H.; Grana, A., and Vaghi Mosquera, D.: Parálisis transitorias de los nervios oculares de naturaleza alérgica, An. Fac. med. de Montevideo **26**:1026, 1941.

girl, had variable transitory episodes of extraocular-muscle paralysis associated with exophthalmos and conjunctival and palpebral edema, which was observed for more than a year and ultimately subsided without any residual extraocular-muscle pareses.

Variable external ophthalmoplegia constitutes a syndrome which may occur as the result of a variety of causes. A parasellar intracranial aneurysm is being increasingly considered as a relatively frequent source of variable ophthalmoplegia. Ophthalmoplegic migraine is well known and has sometimes been thought to be allergic.

Myasthenia gravis must certainly be included as a very common, if not the commonest, cause of variable ophthalmoplegia. Thyropituitary endocrinopathy may produce such pareses of extraocular muscles. Cyclic paralysis of the oculomotor nerve is an interesting clinical syndrome, characterized by alternate phases of spasm and relaxation of the pupil and extraocular muscles in the distribution of the oculomotor nerve. Hicks and Hosford [14] have outlined the essential features of this syndrome and reviewed all the cases prior to 1937. Among other rare causes of ophthalmoplegia are dermatomyositis and scleroderma.

A survey of the literature would lead to the conclusion that angioneurotic edema is a rare, if not the rarest, cause of ophthalmoplegia. In the case here reported the evidence leads inescapably to the conclusion that the variable ophthalmoplegia is due to a peripheral muscular or neuromuscular affection. The complete lack of response to the intramuscular administration of neostigmine in a therapeutic test dose eliminates the diagnostic possibility of myasthenia gravis. The coexistence of variable and palpable edema of the eyelids is a feature which points in the direction of a combined dermatologic and neuromuscular disease process. The frequent exacerbations and remissions, which include complete subsidence of the edema of the eyelids, as well as the pronounced variability in the ophthalmoplegic manifestations, oppose any serious consideration of dermatomyositis and scleroderma, while strongly supporting the diagnosis of angioneurotic edema. Cyclic paralysis of the oculomotor nerve cannot be considered accountable for the ophthalmoplegia in this case because of the coexistence of palpebral edema and the evidence of external rectus pareses at times, as well as the lack of pupillary involvement at any time.

As demonstrated in our case, angioneurotic edema tends to be resistant to therapy unless a specific allergic factor is discovered and can be eliminated. As a rule, epinephrine and ephedrine are ineffective. Spontaneous recovery has been said to occur with advancing age. The prognosis is said to be relatively better in the cases in which hereditary predisposition is lacking.

SUMMARY AND CONCLUSIONS

Ophthalmoplegia as a prominent manifestation of angioneurotic edema may be presumed to be a rare occurrence.

The case is reported of a 25-year-old woman in whom variable ophthalmoplegia was observed to recur irregularly and unpredictably.

The differential diagnosis and treatment are briefly considered.

14. Hicks, A. M., and Hosford, G. N.: Cyclic Paralysis of the Oculomotor Nerve, Arch. Ophth. **17**:213 (Feb.) 1937.

Clinical Notes

A NEW IMPROVED EYE-PARTICLE REMOVER

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EVERY physician is periodically called upon to remove foreign bodies from the eye. A piece of cotton wrapped around a wooden swab is most frequently used to remove the particle.

Figure 1*A* shows a cotton swab under the low-power magnification of the microscope. The rough, irregular projections will increase the irritation of the optic membrane. Figure 1*B* shows a freshly laundered handkerchief under the low-power magnification of the microscope. The sharp, irregular projections will add to the irritation of an already irritated membrane. To overcome these objections, I experimented with a variety of substances and found that a specially smoothened round-wire loop caused the least amount of irritation.

Figure 1*C* shows the specially smoothened round-wire loop under the low-power magnification of the microscope. The perfectly smooth wire surface causes the minimal irritation to the sensitive ocular membrane. An eye-particle remover incorporating this smoothened round wire was described in *The Journal of the American Medical Association.*[1]

The object of the present article is to describe a new improved eye-particle remover which will reduce to a minimum the ocular irritation due to removal of foreign bodies from the eye. To facilitate the removal of metallic particles from the eye, a magnet attracting these metallic particles is incorporated in the instrument. General Electric Company's Alnico No. 5 was chosen because it is the strongest permanent magnet made.

In order to reduce the pressure and consequent injury to the sensitive tissue, the idea was developed of transferring this pressure from the eye to a spring, or a series of springs, on the wire loop itself. As a result, various numbers, shapes, and sizes of springs were constructed.

These variously constructed wire loops were tested in both private and clinic practice by Dr. Donald Lyle and the Department of Ophthalmology of the Cincinnati General Hospital. The ideal construction, causing the least amount of ocular irritation and, at the same time, functioning properly, was found to consist of a double loop of wire placed on two sides of the loop adjacent to the magnet (Fig. 2*B*).

Figure 2*A* shows the eye-particle remover closed; *B*, the eye-particle remover open.

The plastic magnifying lens will not break when dropped and has a magnifying power of 18 D. The stem of the magnifying lens protects the wire loop, and the magnifying lens helps to locate the particle. The specially smoothened rounded-wire loops are constructed of a rustproof material so that they can be sterilized. The loop is held firmly in place by having its open ends bent beneath the magnet, while the magnet and the wire loops are held in position by heat sealing the plastic handle.

1. Biederman, J. B.: Preliminary Report on a New Eye Particle Remover, J. A. M. A. **118**:802 (March 7) 1942.

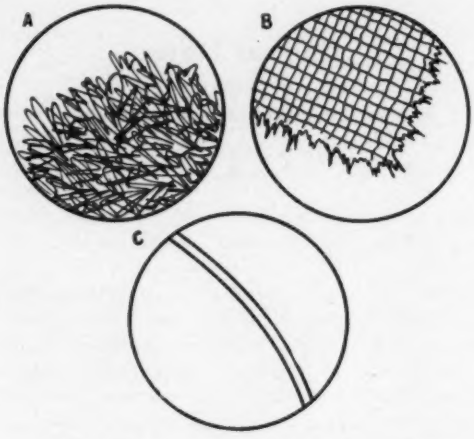

Fig. 1.—*A*, cotton swab under the low-power magnification of the microscope; *B*, freshly laundered handkerchief under the low-power magnification of the microscope; *C*, specially smoothened round-wire loop under the low-power magnification of the microscope.

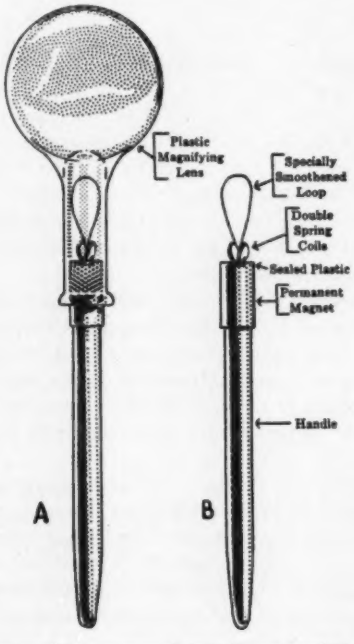

Fig. 2.—*A*, eye-particle remover closed; *B*, eye-particle remover open.

COMMENT

The longer a foreign body remains in the eye, the more damage will result and the more difficult it becomes to remove the substance. Consequently, the eye particle should be removed as soon as possible. For large, deeply embedded metallic particles, larger magnets should be used. The eye-particle remover here described is a useful instrument to have on hand for removal of both metallic and nonmetallic superficial foreign bodies. If the particle happens to be magnetizable metal, the magnet attracts the metal and facilitates its mechanical removal by the loop. If the foreign body is not metallic, the specially smoothened, spring-constructed wire loop will mechanically remove the particle with the least amount of trauma.

SUMMARY

A new improved eye-particle remover is described. It consists of a plastic magnifying lens to help locate small particles. A permanent magnet loosens and attracts small, superficially located, magnetizable metal particles. The specially smoothened round wire with a spring construction removes the foreign body with the least amount of trauma.

METHYL CELLULOSE SOLUTION FOR OPHTHALMIC USE

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THE USE of methyl cellulose solutions in ophthalmology is growing daily.[1] Because there is a variation in the concentrations recommended for use, as reported in the literature, my associates and I have tried to determine the concentration of methyl cellulose which would be most satisfactory and the proper composition of solutions of this substance. It also seemed advisable to investigate further the physical stability of solutions of methyl cellulose. Our findings are presented below.

CONCENTRATION OF SOLUTION

After trying the recommended 4,000-centipoise methyl cellulose in various strengths, I found that the 0.33 + % solution was the most satisfactory as a tear substitute. Concentrations of 0.25, 0.5, and 1% proved either too thin or too thick.

THE VEHICLE—pH AND TONICITY

The methyl cellulose was tried in various vehicles, as it is necessary to make the solution isotonic because the large methyl cellulose molecule exerts practically no osmotic pressure. Isotonic sodium chloride solution was quite satisfactory, although somewhat variable in the sensation it would produce when instilled. A mixture of equal parts of Hind and Goyan's phosphate buffer [2] solution and isotonic sodium chloride solution has been more satisfactory. This solution has a pH of about 6.9 and should be more satisfactory than a more alkaline solution. The concentration of benzalkonium (zephiran®) chloride in the final solution should probably not exceed 1 : 50,000 because of the longer contact with the cornea after viscous solutions are instilled. The methyl cellulose solution made up from the buffer and saline will not have a softening effect on proteins of the conjunctiva, as a more alkaline solution would. The solution should be more stable, better preserved, and slightly antiseptic when made with the phosphate buffer. It is with the solution containing the buffer that I have had the most gratifying results. Except as a vehicle for salts of alkaloids, a solution of pH 7 to 7.2 would probably be equally satisfactory, but it has proved more feasible to have the druggist use the already available Hind and Goyan's buffer and isotonic saline in equal parts. The complexity of the usual dispensing problem is, therefore, not increased over that presented by Martin and Mims.[3]

VEHICLE FOR ALKALOIDS

Methyl cellulose solutions make excellent vehicles for the alkaloids used in ophthalmology. The same reasons for buffering these solutions, and buffering them at a pH of about 6.8 to 6.9, apply here as they do to simple aqueous solutions.[3]

From the Department of Ophthalmology, University of Texas Postgraduate School of Medicine, San Antonio Division.

1. Swan, K. C.: Uses of Methyl Cellulose, Arch. Ophth. **33**:378-380 (May) 1945.

2. Hind, H. W., and Goyan, F. M.: New Concept of the Role of Hydrogen Ion Concentration and Buffer Systems in Preparation of Ophthalmic Solutions, J. Am. Pharm. A. (Scient. Ed.) **36**:33-41 (Feb.) 1947.

3. Martin, F. N., Jr., and Mims, J. L., Jr.: Preparation of Ophthalmic Solutions with Special Reference to Hydrogen Ion Concentration and Tonicity, Arch. Ophth. **44**:561-572 (Oct.) 1950.

However, the tears do not so quickly dilute these more viscous solutions; hence less buffering power is needed in a solution of methyl cellulose to be used for salts of alkaloids. For this reason, the use of equal parts of isotonic sodium chloride solution and Hind and Goyan's phosphate buffer solution was considered as a vehicle for alkaloids and found to be satisfactory.

STABILITY OF METHYL CELLULOSE SOLUTIONS

Since methyl cellulose will dry and form a pliable, flaky deposit in the lashes if used to excess, the question arose whether the methyl cellulose might form deposits in the lacrimal passages and block normal tear drainage. Methyl cellulose solutions of varying percentages (0.25, 0.33 +, 0.5, and 1) were placed in a water bath at body temperature. These were inspected at 15-minute intervals for two hours without cooling. They were also left to stand at room temperature for several days. Although methyl cellulose is more soluble in cold then in hot solutions, the methyl cellulose did not come out of solution at body temperature. If the solution is autoclaved, the methyl cellulose will always separate out as globules, but return readily to solution on standing at room temperature.

Our pharmacists have had no trouble in preparing methyl cellulose solutions from the commercially available powder of the pharmaceutical grade of the 4,000-centipoise type. One-third of the total volume of solvent to be used is heated to about 170 F. The methyl cellulose is allowed to soak in this for 30 minutes. The remaining solvent is placed in a refrigerator to cool to 40 F. during the time required for the soaking process. The methyl cellulose will easily go into a solution when the cold solvent is then added. The use of hot solution for soaking, followed by adding cold solution for the final preparation, is the secret of preparing these solutions easily. If the methyl cellulose preparation is allowed to stand in a refrigerator at 40 F. for a few hours, any remaining cloudiness will always clear up.

USES

Methyl cellulose solutions when prepared as outlined above have had their greatest application in the following situations: (1) in replacing the deficient tear secretion found in postmenopausal women and in many men over 50 years of age; (2) in the postenucleation socket as a lubricant for the prosthesis; (3) as a protective medication for pathologic conditions of the cornea of various sorts (it helps to relieve discomfort in such diseases as band form keratitis, endothelial-epithelial dystrophy, and old healed trachomatous pannus); (4) after tonometry (ephedrine sulfate, 0.1%, is added to the solution used for this purpose, unless, of course, the intraocular tension is elevated).

SUMMARY

Methyl cellulose solutions are providing a valuable addition to our therapeutic armamentarium. Various observations on the preparation of solutions of methyl cellulose, their stability, and uses are presented.

Registry of Interesting Cases

It is the purpose of this section to record cases on the basis of interest only. No complete review of the literature is attempted and no claim for priority is implied except when specifically stated. Publication of case reports is subject to the concurrence of the Editorial Board on the interesting aspects of the case. It is requested that the reports submitted be as brief as is consistant with inclusion of the pertinent facts, bear a title that is as specific as possible, be prefaced by a paragraph that states why the author feels the case is of interest and be accompanied with photographs whenever possible.

MALIGNANT MELANOMA ASSOCIATED WITH RETINAL HOLE

Sir William Lister [1] made the statement years ago that the presence of a hole in the retina with a detachment ruled out the possibility of a malignant melanoma. Duke-Elder,[2] in his latest edition, remarks that the statement has never been contradicted. This case is presented to demonstrate that the two conditions can appear simultaneously.

Mr. M. H., aged 52, in apparent good health, was first seen on Jan. 5, 1950, with the history of a shadow before the right eye associated with occasional flashes of light, of two-weeks' duration. These was a vague history of his striking his head upon entering an automobile several days prior to the appearance of the visual symptoms. The patient had been told of a "scar" on the retina at a previous examination, in July 1949.

The refractive error was found to be as follows:

O. D.: -0.25 sph $\bigcirc$ $+0.75$ cyl, ax 88 20/20 — 2
O. S.: $+0.25$ sph $\bigcirc$ $+0.25$ cyl, ax 90 20/20
Add $+2.25$ sph. Reads metric 1

External examination revealed nothing abnormal. The pupils were round, regular, and active. The muscular balance was normal except for 3 D. of exophoria for near. Slit-lamp examination revealed no pathology in the anterior segment. The intraocular pressure was 23 mm. Hg (Schiøtz) in each eye. The media were clear. The fundus of the left eye was essentially normal. A bullous detachment of the retina was seen extending from 9:30 to 1 o'clock, involving the upper two-thirds of the temporal retina in the right eye. The detachment did not include the macular area. The region above the macula was slightly suggestive of a solid detachment. A large horseshoe tear was seen in the retina in the 10 o'clock meridian. Several large, dark opacities were seen in the midvitreous. Transillumination revealed nothing abnormal. Determination of the visual field revealed a defect comparable to the detached area.

On Jan. 9 diathermy was performed. The postoperative course was uneventful. The hole appeared to be sealed, but the perimacular area remained slightly elevated and a scotoma corresponding to its shape was present. The patient was discharged from the hospital on Jan. 27, wearing pinhole glasses. On Feb. 1 vision again became very blurred and the retina extensively detached. The original hole appeared to be closed, but a smaller tear was seen above it. The patient was readmitted to the hospital and a second diathermy performed on Feb. 8, but the retina remained extensively detached. Because of the possibility of malignant melanoma in the posterior pole, it seemed advisable to remove the eye. Enucleation was done on March 15.

Pathological Report.—Macroscopic Study: A tumor of the choroid, measuring 5 by 25 mm., is visible in the posterior pole.

Microscopic Study: The anterior segment appears normal. The globe is collapsed, and the relative positions of the internal tunics are somewhat altered.

1. Lister, W.: Holes in the Retina and Their Clinical Significance, Brit. J. Ophth. **8**:1 (Jan.) 1924.

2. Duke-Elder, W. S.: Text-Book of Ophthalmology, Vol. 3, St. Louis, C. V. Mosby Company, 1940, p. 2907.

The retina is detached throughout most of its extent, but the small amount of subretinal fluid indicates that this detachment is an artefact. The retina is disorganized and atrophic on both sides from the ora serrata to the region of the equator. On one side in the equatorial region a hole in the retina is visible in some sections. In other sections this hole is closed by scar tissue caused by diathermy applications. The sclera overlying this area contains a number of foci of chronic inflammatory cells, which reveal the area treated.

The choroid just posterior to this treated area, in the sclera, is the site of a small tumor. The tumor is composed of a mixture of an epithelioid type of nevus cells and spindle cells. It is relatively melanotic.

Diagnosis.—The diagnosis is malignant melanoma (neurogenic type, fiber group III); detachment of the retina following a tear, and diathermy for retinal detachment.

SUMMARY

This case seemed worth reporting, as it demonstrates well the association of detachment of the retina with a tear and a malignant melanoma. The original picture was one of apparent uncomplicated detachment of the retina with a hole. After diathermy the hole was sealed and the retina reattached. A second hole developed, and the retina again became detached. The ultimate finding was that of malignant melanoma. One assumes that the detachment was secondary to the malignant melanoma. However, on examination of this small, flat tumor, one wonders whether this could have caused the detachment or whether the lesions were coincidental in the same eye. It is hard to associate the peripheral retinal tear with the small tumor in the macular area.

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Ophthalmological Reviews

OCCLUSION OF THE CENTRAL RETINAL VEIN

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ALTHOUGH occlusion of the central retinal vein is a commonly seen clinical entity, separated from the group of so-called hemorrhagic retinopathies over 70 years ago, there has been no universal agreement concerning its etiology or pathogenesis. This is well illustrated by the numerous forms of treatment which have been employed and the conflicting reports of their success.

The first published report of the pathologic findings in occlusion of the central retinal vein was that of von Michel,[1] who described two cases in 1878 and reported a third 21 years later. He suggested that the occlusion in his first case might be due to proliferation of the intima, but ascribed the occlusion to thrombi in the other two cases. In the next 25 years 20 more cases were reported,[2] in 10 of which thrombi were stated to be the cause of the occlusion. One showed proliferation of the endothelium, and nine were reported as having normal central retinal veins.

In 1904 Coats [2] described four cases, in three of which he thought the cause was thrombosis, and in one, endothelial proliferation. He reviewed all the cases reported up to that time and concluded that the occlusion was due to thrombosis of the central retinal vein superimposed on the vascular changes of angiosclerosis. Coats expressed the belief that the underlying venous disease might be due to strain, aging, nephritis, syphilis, or an unusual course of the vein and pointed out that Hertel had found endothelial and subendothelial proliferation in eyes that ophthalmoscopically were without evidence of angiosclerosis. Though Hertel dealt chiefly with arteries, Coats believed that the same changes occurred in veins and that intimal proliferation, connective tissue proliferation of the media, and hyaline degeneration were all factors which favored thrombosis. He noted the occurrence of obstruction of the central retinal vein in mitral stenosis and attributed it to the interference with venous return, predisposing to thrombosis. The new channels in the obstructed veins were interpreted by him as representing canalization of thrombi, by means of which the venous return was reestablished, at least in part.

Harms,[3] in 1905, also considered the obstruction to be due to thrombosis and pointed out the importance of making serial cross sections, instead of longitudinal

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1. von Michel, J.: Die spontane Thrombose der Vena centralis des Opticus, von Graefes Arch. Ophth. **24**:37, 1878; Über Erkrankungen des Gefässystems der Arteria und Vena centralis retinae mit besonderer Berücksichtigung der pathologisch-anatomischen Veränderungen, Ztschr. f. Augenh. **2**:1, 1899.

2. Coats, G.: Thrombosis of the Central Vein of the Retina, Roy. London Ophth. Hosp. Rep. **16**:62, 1904.

3. Harms, C.: Anatomische Untersuchungen über Gefässerkrankungen im Gebiete der Arteria und Vena centralis retinae und ihre Folgen für die Cirkulation mit besonderer Berücksichtigung des sog. hämorrhagischen Infarktes der Netzhaut, von Graefes Arch. Ophth. **61**:245, 1905.

sections, through the region of the lamina cribrosa in order to determine the nature of the occlusion and its relations to the vessel wall.

In 1906 Verhoeff [4] reviewed 39 previously described cases, including those of Coats, and concluded that in only 2 was there actual anatomic proof of thrombosis and that in both these cases it occurred as a result of sepsis. In only 12 cases was there adequate evidence that the obstruction had been sufficient to cause the retinal changes, and in none of these was there evidence that the obstruction was not due entirely to proliferative endophlebitis. In this article Verhoeff reported six cases of his own and described the retinal changes, which consisted of edema in the external plexiform layer with large cystic spaces, especially in the macular region, and hemorrhages, most numerous in the nerve fiber layer and internal nuclear layer, sometimes extending into the external plexiform layer. In one case the central retinal vein showed intimal proliferation of either endothelial or subendothelial cells, forming a fibrous layer with many reticular spaces, and collapse of the vein, due to contraction of the fibrous tissue. The spaces in the reticulum were continuous with small collaterals of the vein. In his second case there was similar intimal thickening, with endothelial cells proliferating into the lumen of the vessel. The degenerated intima was hyalinized. A collateral vein entered the intima, forming two endothelium-lined spaces, which communicated with the original lumen and each other. His other four cases were similar. Verhoeff stated that the processes in this condition are (1) intimal proliferation and hyaline degeneration; (2) proliferation of the endothelium into the lumen of the vein, and (3) subsequent undermining of the degenerated intima by the blood stream of a small collateral, with new endothelium derived from the collateral lining these new spaces. Previous collapse of the vein might play a part in the occurrence of this—the blood from the collateral forcing its way more readily beneath the intima. Verhoeff believed that these processes formed what was called a thrombus by others and that a so-called canalized thrombus was in the nature of a dissecting aneurysm.

Inouye,[5] in 1910, reported a case of occlusion of the central retinal vein due to subendothelial proliferation, supporting Verhoeff's findings.

In 1913 Coats [6] found fibrous thickening of the wall of the vein and concentric constriction of the lumen; he described endothelial proliferation of arteries, but not of veins. In the same year, he reported the pathologic observations in 32 cases of hemorrhagic glaucoma following obstruction of the central retinal vein. In 21 cases he ascribed the occlusion to thrombosis; in 3 cases, to thrombophlebitis secondary to intraocular inflammation, such as choroiditis, and in 1 case, to concentric thickening of the wall of the vein, with gradual closing off of the vessel. In six cases he found endothelial proliferation but thought that this was a secondary process, with endothelial cells proliferating into a preexisting thrombus.[7]

4. Verhoeff, F. N.: Obstruction of the Central Retinal Vein, Ophth. Rev. **25**:353, 1906; Obstruction of the Central Retinal Vein, Arch. Ophth. **36**:1, 1907.

5. Inouye, T.: A Case of Obstruction of the Central Vein and Glaucoma, with Remarks, Roy. London Ophth. Hosp. Rep. **18**:1, 1910.

6. Coats, G.: Discussion on Retinal Vascular Disease: Pathological Aspects, Tr. Ophth. Soc. U. Kingdom **33**:30, 1913.

7. Coats, G.: Der Verschluss der Zentralvene der Retina: Eine Übersicht 36 pathologisch-anatomisch untersuchter Fälle, von Graefes Arch. Ophth. **86**:340, 1913.

Moore,[8] in his monograph in 1924, without any histologic evidence of his own, expressed the belief that occlusions of the central retinal vein were due to thrombosis, and stated that the venous return after occlusion was maintained by devious routes until opening of collateral channels and canalization of the blocked vein occurred. He emphasized the importance of chorioretinal anastomoses, citing Leber's statement that anastomoses between choroidal and central retinal veins around the disk take three directions: (1) backward to the pial sheath—the chorio-vaginal veins; (2) straight inward to the lamina cribrosa, forming opticociliary veins, and (3) forward to the papilla to take part in its vascularization, these anastomoses, when enlarged and tortuous, forming cilioretinal veins.

Gradle,[9] without presenting any evidence, suggested that three factors are of importance in occlusion of the central retinal vein: (1) reduction in the caliber of the central retinal artery, due to syphilis, arteriosclerosis, or a sclerosing process of the lamina, which, by mechanical choking of the artery, leads to slowing of the blood flow; (2) a rough spot on the endothelium, due to toxic endophlebitis or mesophlebitis, leading to endothelial proliferation or fibrin deposit, and (3) emergence of the central retinal vein from the nerve immediately behind the globe, instead of 7 to 15 mm. posterior to the lamina, so that the central retinal vein undergoes two sharp bends instead of a gradual curve of emergence, thus leading to slowing of the blood stream. Gradle also suggested that a preglaucomatous state existed in some cases, in which the altered intraocular circulation precipitated an acute hypertensive attack, with glaucoma developing in the unaffected eye at a later date.

Klien,[10] on the other hand, reporting on the study of 21 eyes lost because of glaucoma following obstruction of the central retinal vein, agreed with Verhoeff, finding endothelial and subendothelial proliferation and dissecting aneurysms. She found that in occlusion associated with systemic disorders, the site of most extensive endothelial proliferation frequently was in the anterior level of the lamina cribrosa, or even in the prelaminar region near the junction of the papillary veins, and was always associated with pronounced narrowing of the vein in the posterior level of the lamina, due to mesophlebitis and encroachment on the vein by neighboring sclerotic structures. This suggested a partly mechanical origin of the endothelial proliferation, perhaps due to narrowing of the venous aperture farther back. A prerequisite for ensuing endothelial proliferation would be a lack of normal resistance, such as occurred in systemic diseases or senility. Klien found that with advanced age, without hypertension or other disease, the obstruction was in the posterior level of the lamina, in which the final event was irritative endothelial proliferation due to extreme compression at the angles of a semilunar space. She was also of the opinion that in the case of preexisting arterial disease occlusion of the central retinal vein caused stagnation, retrograde slowing of the blood flow, and subsequent occlusion of the central retinal artery in a short time. Klien also pointed out the thin-walled preretinal collaterals and dilated preformed venous or capillary

8. Moore, R. F.: Retinal Venous Thrombosis: A Clinical Study of 62 Cases Followed over Many Years, London, George Pulman and Sons, Ltd., 1924.

9. Gradle, H. S.: The X-Ray Therapy of Retinal-Vein Thrombosis, Am. J. Ophth. **20**:1125, 1937.

10. Klien, B. A.: Obstruction of the Central Retinal Vein, Am. J. Ophth. **27**:12, 1944.

channels within the nerve at the level of the lamina and stated the belief that the degree of optic nerve atrophy following obstruction of the central retinal vein depended on the efficiency of the collateral circulation, in the presence of which secondary glaucoma might exist for a long time without inducing extensive destruction of nerve elements. Without collaterals, rapid optic nerve atrophy developed, owing to a combination of malnutrition and toxic action, to which only much later the destructive influence of elevated tension was added. In younger patients, Klien found that no fibrosis of the central connective tissue strand took place and that endothelial proliferation occurred in the posterior half of the lamina. She stated that the rapidity and efficiency with which collaterals develop depend on preexisting channels and the rate of obstruction of the central retinal vein. In younger patients, with hypertension, diabetes, or syphilis, the occlusion was due to more widespread, but less complete, venous circulatory embarrassment than in older patients with senescence alone, and therefore that therapeutic results were better in the former.

Harms [3] and Leber [11] thought that arteriosclerosis of the central retinal artery caused slowing of the blood flow, which resulted in thrombus formation. Reimar [12] stated that temporary slowing or obliteration of arterial flow caused occlusion of the central retinal vein, that the arterial circulation was then restored, and that profuse retinal hemorrhages then occurred through the venous walls already damaged by anoxia—the "stagnation thrombus" of Klien.[10] Harms,[3] Moore,[8] Klien,[10] and Gradle,[9] as already mentioned, believed that congenital vascular anomalies were important factors, as was tortuosity of vascular loops on the disk.

McLean,[13] in discussing anticoagulant therapy in occlusion of the central retinal vein, stated that in none of the eyes enucleated for hemorrhagic glaucoma which he examined microscopically could he find evidence of endothelial proliferation and that, according to general pathologists, endothelial proliferation never occurs in veins elsewhere in the body, though it does occur in arteries; the thickened artery, encroaching on and indenting the vein, may supply the irritation or cause of the endothelial roughening which initiates thrombosis. From studies made with Rich, he was convinced that the underlying factor in occlusion of the central retinal vein is thrombosis. However, neither McLean nor Gradle [9] presented cases or gave any proof of their contentions.

Verhoeff [14] demonstrated that chronic glaucoma may produce endovasculitis of the central retinal vessels with the same changes that he had previously described in hemorrhagic glaucoma—endothelial and subendothelial proliferation and formation of new channels by dissecting aneurysms. He did this by examining the central vessels in 39 eyes with glaucoma secondary to obstruction of outflow. He found that the age of the patient was not an essential factor. In these eyes, however, the occlusion was slow in developing and seldom, if ever, produced the intense

11. Leber, T.: Die Thrombose der Zentralvene und die hämorrhagische Retinitis, in Graefe, T., and Saemisch, T.: Handbuch der gesamten Augenheilkunden, Leipzig, W. Engelmann, 1915, Vol. 2, p. 355.

12. Reimar, M.: Über Retinitis hämorrhagica infolge von Endarteritis proliferans mit mikroskopische Untersuchung eines Falles, Arch. Augenh. **38**:209, 1899.

13. McLean, A., in discussion on McLean, A. M., and Solanes, M. P.: Anticoagulant Therapy in Retinal Vascular Occlusion, Tr. Am. Acad. Ophth. & Otol., p. 644, July-Aug., 1949.

14. Verhoeff, F. H.: Effect of Chronic Glaucoma on the Central Retinal Vessels, Arch. Ophth. **42**:145, 1913.

hemorrhagic retinopathy found with primary occlusion. In fact, of the 15 eyes with complete, or almost complete, venous occlusion, there were retinal hemorrhages in only 3, and in only 1 of these were there more than a few. Verhoeff attributed the absence of extensive retinal hemorrhages in these cases to coincident marked involvement of the artery, the slowness of the process, and the development of a collateral circulation in the optic nerve. He believed that the vascular changes in secondary glaucoma were dependent on a direct action of the increased intraocular pressure. Scheerer,[15] in 1922, then unaware of Verhoeff's work, independently reported similar changes in the central retinal vessels, both in primary glaucoma and in hemorrhagic glaucoma, and two years later confirmed Verhoeff's finding of loss of connective tissue substance at one point along the central retinal vein, with proliferation of neuroglia against the venous wall, producing an invagination of the venous wall before it and partial collapse of the vessel. Scheerer was able to demonstrate at the anterior end of the central venous trunk the existence of a collateral circulation by which the occurrence of retinal hemorrhages in occlusion of the central retinal vein could be prevented or delayed. The importance of the collateral circulation about the disk was first pointed out by Verhoeff [14] and later emphasized by Moore,[8] Klien,[10] and Ballantyne.[16]

Salzmann,[16a] in 1933, examined 65 eyes enucleated for glaucoma. He agreed with Verhoeff, finding complete obstruction of the central retinal vein in 18 eyes and changes in the central retinal vein in 75% of the eyes.

Occlusion of the central retinal vein has been reported accompanying or following diseases other than diabetes, hypertension, arteriosclerosis, and syphilis. Verhoeff and Simpson [17] published a case of clear-cut hemorrhagic glaucoma in which the eye on section showed a tubercle in the central retinal vein, with tuberculous periphlebitis retinalis in the other eye. Sáfar [18] and Friedenwald [19] reported similar cases. Moore [8] noted the presence of occlusion of the central retinal vein in young patients with influenza, and Brændstrup [20] mentioned its occurrence in septic processes involving the orbit or paranasal sinuses and in cavernous sinus thrombosis, facial erysipelas, and ophthalmic herpes zoster. Occlusion of the central retinal vein has been reported in cases of direct ocular trauma,[21] and after rubbing the eye,[20] and Brændstrup [20] described a case in which occlusion developed on sudden

15. Scheerer, R.: Zur pathologischen Anatomie der Veränderungen der Netzhautzentralgefässe bei der sogenannten Thrombose der Zentralvene und Embolie der Zentralarteris, von Graefes Arch. Ophth. **110**:292-331, 1922.

16. Ballantyne, A. J.: Observations on the Pathology of Thrombosis of the Central Vein of the Retina, Tr. Ophth. Soc. U. Kingdom **63**:7, 1943.

16a. Salzmann, M.: Glaukom und Netzhautzirkulation, Zentralbl. f. d. ges. ophth. **29**:216, 1933.

17. Verhoeff, F. H., and Simpson, G. V.: Tubercle Within Central Retinal Vein, Hemorrhagic Glaucoma: Periphlebitis Retinalis in Other Eye, Arch. Ophth. **24**:645 (Oct.) 1940.

18. Sáfar, K.: Über Drucksteigerung im Gefolge der juvenilen Netzhaut-Glaskörperblutungen und Verschluss der Zentralvene infolge tuberkulöser Phlebitis, nebst Bemerkungen über die Entstehungsweise der Netzhautgefässtuberkulose, von Graefes Arch. Ophth. **119**:624, 1928.

19. Friedenwald, J., in discussion on Verhoeff and Simpson,[17] p. 652.

20. Brændstrup, P.: Central Retinal Vein Thrombosis and Hemorrhagic Glaucoma, Acta ophth., Supp. 35, pp. 1-159, 1950.

21. Haemig, E.: Schweiz. med. Wchnschr. **2**:933, 1941; cited by Brændstrup.[20] Brückner, R.: Ophthalmologica **109**:203, 1945; cited by Brændstrup.[20]

exposure to a strong wind at sea. It has been reported in cases of congenital heart disease,[6] leukemia,[20] polycythemia,[20] multiple myeloma,[22] and Raynaud's disease.[23]

CLINICAL PICTURE

The clinical features of occlusion of the central retinal vein have been well described by Moore,[8] who followed 62 cases for periods ranging up to 30 years, and by Brændstrup,[20] whose observations are based on 131 cases, the largest series published to date.

The disease is one of middle age, with the peak incidence in the seventh decade; it occurs oftener in men than in women, and the left eye is more frequently involved than the right. The presenting symptom in most cases is sudden loss of vision, described as dimness or mistiness. Moore found the visual acuity rarely such as to permit useful vision, and in all cases the vision became progressively worse; Brændstrup, however, found that 25% of patients maintained a visual acuity of 6/18 or better, and 50% had an acuity of 6/60 or better. All patients who maintained an acuity of 6/18 or better were under 54 years of age. There was no correlation between the visual acuity and the severity of the morphological changes.

Visual field findings are variable; the peripheral fields may remain nearly full for years, or they may become markedly constricted in five days; in time, however, irregular constriction occurs, and a central or paracentral scotoma is probably always present. Moore found the tension to be lower in the affected eye than in the normal eye in cases in which hemorrhagic glaucoma did not later develop, and he believed that this was of prognostic significance. The earliest ophthalmoscopic finding is retinal edema, appearing first along the large veins and then spreading throughout, being most prominent at the posterior pole. The veins become greatly dilated and tortuous, and there are profuse retinal hemorrhages, both superficial and deep. Preretinal hemorrhages may occur. Venous microaneurysms are seen. Brændstrup found "cotton wool" patches in 54% of his cases, in proximity to the hemorrhages. The disk is hyperemic and may be edematous, but never strikingly so. With the passage of time the veins become somewhat less tortuous and show sheathing. The arterioles show pronounced arteriosclerotic changes and may acquire pipestem sheathing. The edema subsides; the cotton wool patches become more sharply delimited and are absorbed. Moore stated that hemorrhages either recur or persist, but Brændstrup found all hemorrhages to be absorbed within two years. In the majority of cases, the disk does not become atrophic, but resumes a normal appearance with numerous anastomoses and new-formed vessels. Moore noticed new vessels on the disk as early as six weeks after the occlusion. The only retinal lesions found in old cases are small, white-gray, irregularly scattered patches, and granular changes at the macula resembling those of senile macular degeneration. Brændstrup concluded that the poor vision was undoubtedly due to the macular degeneration.

Moore reported that the life expectancy of patients with occlusion of the central retinal vein was poor, survival after the venous occlusion being about 5.8 years, and death being due to hypertension or cerebral vascular accidents; Brændstrup,

22. Eskildsen, P.: Nord med. **14**:1395, 1942; cited by Brændstrup.[20]

23. Wintrobe, M. M., and Buell, M. V.: Hyperproteinemia Associated with Multiple Myeloma, Bull. Johns Hopkins Hosp. **52**:156-165, 1933.

however, found no shorter life expectancy than in normal persons in this age group. The major complication of occlusion of the central retinal vein is hemorrhagic glaucoma, which occurs in 5 to 23% of cases.[24] The average interval between the vascular accident and hemorrhagic glaucoma is 3 to 6 months,[20] but it has been reported as early as 13 days [6] and as late as one year.[20]

SUMMARY AND CONCLUSIONS

Since its first description, there have been two opposing schools of thought concerning the nature of the obstruction in occlusion of the central retinal vein. Coats and others have contended that the obstruction is due to a true thrombosis, similar to thromboses occurring elsewhere in the vascular tree, and that the thrombi may become canalized, as occurs in venous thromboses in other organs. Verhoeff, however, has demonstrated that the occlusion may be due to endothelial and subendothelial proliferation, with closure due to contraction of the new-formed connective tissue and endothelial proliferation into the lumen of the vein. He also demonstrated that there is degeneration of the intima, with undermining of the degenerated intima by the blood streams of small collaterals of the vein, thus forming new channels, which receive their endothelial lining from the venous collaterals; that is, the recanalization of the occluded vein is really due to a process similar to that of a dissecting aneurysm.

It would appear that both conditions occur. In elderly arteriosclerotic patients, with or without hypertension, who comprise the majority of persons affected, it would seem that the occlusion is due to endothelial and subendothelial proliferation. On the other hand, in cases associated with orbital or systemic infections or with septic emboli it is probable that thrombophlebitis exists. This is true also for hematologic diseases, such as leukemia, polycythemia, and those occurring after trauma.

This assumption is supported clinically by the strikingly better prognosis in the younger age groups, recovery of vision here presumably being due to canalization of true thrombi. It is in this group that one might expect benefit from anticoagulant therapy. However, in the elderly patient, whose occlusion is usually on an entirely different basis, the rationale for the use of anticoagulants would not seem to be valid. Unfortunately, the ophthalmoscopic findings are not helpful in determining the nature of the obstruction; this decision must be made on the basis of the patient's age and the presence of coexisting disease.

ABSTRACT OF DISCUSSION

Dr. Angus L. MacLean, Baltimore: Dr. Mancall's excellent presentation is extremely timely or, may I say, long overdue. In view of the general acceptance of anticoagulants as valuable agents in the treatment of thrombosis, it is imperative for ophthalmologists, if their patients are to have the benefit of these substances, to decide once and for all whether occlusion of the central retinal vein is due primarily to proliferation of the endothelium or to thrombosis.

Dr. Mancall has made a careful review of all the important papers which have appeared in the literature on this subject. From what one can gather, it is the accepted opinion of pathologists that from none of these reports can the etiology and mechanism

24. Duke-Elder, S.: Text-Book of Ophthalmology, Vol. 3, St. Louis, C. V. Mosby Company, 1940, p. 2585. Moore.[8] Leber.[11] Brændstrup.[20]

of occlusion of the central retinal vein be decided beyond the question of a doubt. The duration between onset of the obstruction and enucleation in each case was so long that no one could say definitely, from a study of microscopic sections, just what was the origin of the plug of connective tissue at the site of the occlusion. Coates's case came nearer to being ideal for such determination than any which has appeared before or since. Coates believed that the microscopic changes were typical of those resulting from thrombus formation with subsequent recanalization and replacement by fibrous connective tissue. This has been the accepted opinion of most pathologists and ophthalmologists. Verhoeff, on the other hand, found no evidence of thrombosis in Coates's case, and in this as well as in photomicrographs of a similar case of his own, endeavored to show that the obstruction was due primarily to proliferation of the endothelium. It therefore became a question of one man's opinion against another's, or really "against the field." A strong point against Dr. Verhoeff's belief is the well-established fact that nowhere else in the body has endothelial proliferation in veins, sufficient to occlude the lumen, been seen or known to occur.

As Leber has stated, however, the question should be considered not only from a pathologic, but also from a clinical, standpoint. We have, I am sure, all seen occlusions, both of branch veins and of the central vein, clear up completely, or almost completely, with restoration of normal, or almost normal, central vision. It is hard to understand how such improvement could occur if the vein were completely occluded and the lumen obliterated by organized endothelial proliferation and ingrowth. One could, however, visualize improvement if the blocking were due to a thrombus. Conditions being favorable, nature can remove thrombi by a process of gradual absorption and washing away of the clot or by recanalization, but cannot remove organized connective tissue.

In his summary, Dr. Mancall has divided the cases into two groups on the basis of age. Apparently on the assumption that infections, toxic processes, tissue hypersensitivity, and blood dyscrasias occur only in the young, he has given this age group over to the adherents of thrombosis, to be treated with anticoagulants, but has retained the older age group for adherents of the theory of endothelial proliferation, to be protected from anticoagulants. These ideas seem somewhat at variance with the accepted ideas concerning the clinical use of anticoagulants. In the presence of infection, anticoagulants should always be administered with caution. Antibiotics and desensitization therapy should probably always be given primary consideration. In dealing with the central vein, however, time is important, and use of anticoagulants should probably be started at once. In thrombocytopenic purpura, leukemia, and the anemias, anticoagulants are contraindicated. In polycythemia, however, they are not contraindicated and are often of extreme value. I have had my most gratifying results with anticoagulant therapy in the older age group and in those patients in the younger age group in whom no obvious cause for the occlusion was found. I believe, unless there are contraindications, such as those just mentioned, that all patients with occlusion of central vein should be given the benefit of anticoagulant therapy and that this should be continued on a conservative basis until all signs of the occlusion have cleared or until it can be determined with certainty that no improvement need be expected from further continuance of treatment and that the outlook is hopeless.

Dr. F. H. Verhoeff, Boston: Dr. Mancall has given an excellent and concise review of the high spots of the literature on occlusion of the central vein. Since the advent of anticoagulant therapy, the question as to the nature of the occlusion is no longer merely academic. My views on the subject are the same as those I expressed in 1906, and I agree with the main conclusions reached by Dr. Mancall. At that time my conclusions were based on my own microscopic observations on six eyes and on the findings in 39 cases reported in the literature. I emphasized the importance of making serial cross sections and brought forward a new method of preparing serial celloidin sections. Subsequently, I made serial cross sections of the central vessels in 221 available eyes removed for primary or hemorrhagic glaucoma. I completed

these examinations about 20 years ago. In addition, I have examined, also in serial cross sections, the central vessels in many cases of secondary glaucoma, including the 39 cases I reported in 1913. No one else has even yet approached this experience. Of the 221 eyes, the central vein was normal in only 15; the artery, in only 10. In 134 eyes the vein, and in 67 eyes the artery, was completely occluded, and in 52 eyes both vessels were completely occluded. I mention these figures simply to show that my material for study has been ample. In not one eye have I found that occlusion of the central vein was due even in part to thrombosis. Commonly, the term "thrombosis" is used as if synonymous with "occlusion" of the central vein. Probably in textbooks and atlases not one fundus illustration entitled "thrombosis of the central vein" is correctly labeled.

In 15 of the 39 cases I collected from the literature in 1906, the central vein was found to be completely patent. This suggests that the clinical diagnosis of occlusion of the central vein, not to mention thrombosis, cannot always be relied upon. I recall one of my own cases which strikingly illustrates this point in a different way. The patient, aged 61, had high blood pressure. In 1915 I removed her right eye for hemorrhagic glaucoma and found the central vein occluded by endothelial proliferation. Two years later she presented herself to me with numerous small retinal hemorrhages in the left eye, retinal edema, and visual acuity reduced to ability to count fingers at 5 ft. (1.5 meters). I felt sure that she then had occlusion of the central vein in this eye. However, she stated that the condition had appeared only two days before, when she leaned out of bed to pick up a clock on the floor. Immediately afterward she saw light flashes, and in the morning her sight was very dim. After one month the hemorrhages were gone and her visual acuity was 20/50. After two months she had recovered her original acuity, 20/30+. She lived six and one-half years after this, without occlusion of the central vein. The retinal hemorrhages were, no doubt, due to a transient great increase in cerebral venous pressure.

I have never denied that under certain conditions, notably those of sepsis, thrombasis of the central vein may occur. Although it has never actually been demonstrated, it is reasonable to assume that it occurs in the rare cases in which young persons with influenza present the fundus picture of occlusion of the central vein, yet recover normal vision. It seems unlikely that the recovery of vision is due to canalization. Probably it is due to shrinkage and disintegration of the thrombus.

As to anticoagulant therapy, to use it after the thrombus was complete would be like locking the stable door after the horse had been stolen. Moreover, it seems to me that the completeness or incompleteness of a thrombus would be determined before anticoagulant therapy could be begun.

Dr. McLean has stated that Prof. Rich supports his contention that occlusion of the central retinal vein is always due to thrombosis. Most general pathologists, however eminent, freely admit that they know nothing about the pathology of the eye. I have been informed that Prof. Rich was asked to discuss this paper but refused on the ground that he knew nothing about the subject.

Annual Reviews

GLAUCOMA

A Review of the Literature 1950-1951

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PHILADELPHIA

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From the Department of Ophthalmology, Hospital of the University of Pennsylvania, the University of Pennsylvania School of Medicine, and the Children's Hospital of Philadelphia.

PRIMARY GLAUCOMA

THE MECHANISM underlying primary glaucoma remains obscure, and the debate regarding its origin continues unabated. In reviewing the literature for 1949-1950, Scheie [1] summarized many of the arguments for and against the mechanical (gonioscopic) and the neurovascular school of thought. The suggestion was made that much of the objection to the gonioscopic school stems from the mistaken idea that it attempts to explain the mechanism of glaucoma. In reality, however, it offers, primarily, a classification of glaucoma which embraces most of the current theories regarding the disease. Adherents of the gonioscopic school assume that the underlying disturbances and physiopathology are largely unproved, thus leaving the subject open for further study. The neurovascular school seems more restricted in its approach to the disease because it arbitrarily assumes a neurovascular origin for all types of primary glaucoma.

I. Mechanism

The gonioscopic classification divides primary glaucoma into two main types, based on the width of the angle of the anterior chamber. Each type runs a characteristic clinical course and shows a different response to treatment. One type invariably is associated with the narrow angle and is referred to as "narrow-angle glaucoma," characterized by acute attacks of congestive glaucoma. The other is associated, in a majority of eyes, with a wide angle and is characterized by a "chronic simple" course.

Acute congestive glaucoma is thought to occur in eyes with narrow angles at times when the iris comes into contact with the trabeculum and prevents filtration of aqueous through that structure and out of the angle. The cause of the narrow angle is unknown, but it probably represents an individual anatomical characteristic. The reason that contact with the trabeculum and closure of the angle occurs is obscure, but several "angle-crowding" factors are known to be involved. These include what appear to be quite purely mechanical factors, exemplified by pupillary dilatation in a dark room, and neurovascular factors, such as those associated with emotional upsets, minor trauma to the eye, and possibly more obscure ones, manifest by an increased rate of aqueous formation, the flow of aqueous pushing the periphery of the iris slightly forward, contact with the trabeculum then occurring.

Chronic simple (wide-angle) glaucoma usually occurs in eyes with wide angles, but exceptions occur in a significant number of eyes in which the angles may be very narrow. All that is implied is that the angle is not closed, the aqueous always having access to the canal of Schlemm. "Open-angle" glaucoma, therefore, is probably a better term. The ocular tension is elevated even though the trabeculum is exposed to the anterior chamber, a condition in contrast to that in narrow-angle glaucoma, in which the tension does not become elevated unless the iris is in contact with the trabeculum to close the angles. The cause of elevated tension, therefore, must include the possibilities of hypersecretion of aqueous, changes in the trabeculum which prevents filtration of aqueous, disease of the efferent or afferent blood vessels of the canal of Schlemm, changes within the canal of Schlemm, alterations in flow through the aqueous veins, and neurovascular disturbances, the specific

1. Scheie, H. G.: Glaucoma: A Review of the Literature, 1949-1950, Arch. Ophth. **44**:883-908 (Dec.) 1950.

nature of which, as yet, is not understood. The gonioscopic school of thought, therefore, while accepting the correlation between angle depth and type of glaucoma, conceives of many different etiological factors. In this way, much of the difference between the two schools of thought can be rationalized and future investigations can be free to pursue any plausible lead.

During the past year, numerous articles on the mechanism of glaucoma have appeared in the literature. For purposes of review, they have been divided into two groups, one supporting the neurovascular school and the other, the mechanical school. The wide variety of causes suggested in these articles, many supported by little objective evidence, serves to emphasize the confused state of our knowledge regarding primary glaucoma. However, this reviewer urges that every reasonable theory be given credence and thoroughly investigated with an open mind, rather than that any one be adopted to the exclusion of others. For this reason, most of the articles are reviewed and sorted into categories.

A. The Neurovascular School.—1. Circulatory Disturbances Within the Eye: Cristini [2] advances histologic evidence to support the neurovascular origin of glaucoma. He found an obliteration of the capillary network in the region of the scleral foramen of glaucomatous eyes which he thought could produce the changes in the lamina, the glaucomatous degenerative halo around the disk, and the degeneration of the optic nerve fibers so characteristic of this disease. He thought that similar changes which he was able to demonstrate in the capillaries of the optic nerve outside the eyeball could explain the optic atrophy and visual-field defects of glaucoma without hypertension because they presumably occurred independent of pressure changes within the eye. He also demonstrated fragmentation and obliteration of the lumina of the vessels of the choriocapillaris, which were severer in more advanced stages of the disease. He suggests that this state of relative, chronic ischemia of ocular tissues may serve as the pathologic basis for the increase in ocular tension by causing a modification of the hemodynamic regimen. He concludes, therefore, that most glaucomatous manifestations, which included visual-field changes and elevated ocular tension, can be attributed to a common vascular pathology. He used normal eyes from persons of comparable age as controls.

In another article, Cristini [3] states that ocular hypertension is due more likely to a rise in capillary blood pressure, and not to an obstruction to the outflow of aqueous. In several patients he demonstrated alterations in the ophthalmic and carotid arteries by cerebral arteriography and suggests that the changes in the small vessels of the eye are related.

Alaerts [4] suggests that chronic glaucoma is due to an increase in choroidal volume occurring on a circulatory basis. He does not accept the premise that obstruction to aqueous outflow may be the cause of elevated tension when the angle is open. He cites the success of fistulizing operations in controlling tension when the wound has apparently sealed over as an argument against obstruction to outflow

2. Cristini, G.: Common Pathological Basis of the Nervous Ocular Symptoms in Chronic Glaucoma, Brit. J. Ophth. **35**:11-20, 1951.

3. Cristini, G.: Nature of Ocular Hypertension in Glaucoma, Proc. XVI Internat. Cong. Ophth., London **2**:865-871, 1950; Etiology and Pathogenesis of Ocular and Extraocular Glaucomatous Symptoms, Bull. sc. med. **123**:7, 1950.

4. Alaerts, L.: Circulation of the Blood and the Aqueous Humor in Chronic Ocular Hypertension, Arch. opht. **10**:613-628, 1950.

as the cause of chronic glaucoma. To the reviewer, this argument is a rather weak one, because diffuse filtration through microscopic fistulae is possible, as indicated by the work of Kronfeld.[5] It is well known, also, that glaucoma in eyes with very narrow angles may be controlled by a simple peripheral iridectomy.

Fritz,[6] in an article somewhat comparable to that of Alaerts, states the belief that the ocular tension varies with capillary pressure. For every 3-mm. increase in capillary pressure, the ocular tension rises 10 mm. He believes that the capillaries have their own pressure-regulating mechanism and that lack of vascular tonus stemming from this mechanism gives rise to glaucoma. He presumes that the mechanism which controls the capillary pressure is under the control of a central nervous mechanism because increased arterial tonus can be eliminated by retrobulbar injection of alcohol, which blocks the ciliary nerves. He feels that atropine increases the capillary pressure for several days, thus accounting for its aggravating effect upon glaucoma, but that pilocarpine has the opposite effect. This paper contains many interesting ideas.

Kraupa[7] also attempts to explain the mechanism of glaucoma on a purely vascular basis. He believes that acute glaucoma occurs on the basis of a static hyperemia, chiefly of the vessels of the ciliary body, with a rise in production of intraocular fluid and a simultaneous reduction in its outflow, with a resultant attack of glaucoma. In chronic simple glaucoma, the disturbance is chiefly in the optic nerve, but when it involves the ciliary circulation high levels of ocular tension occur. Changes in the central nervous system, he believes, can cause these disturbances of the blood flow in the terminal vessels of the eye. He even goes so far as to state that glaucoma secondary to thrombosis of the central vein of the retina and serous iridocyclitis should be called primary glaucoma because they result from the same cause, namely, static hyperemia.

Poos,[8] somewhat similarly, theorizes that glaucoma, including secondary glaucoma and low-tension glaucoma, arises from increased capillary pressure, which causes an increase in volume of the uveal vascular bed. As a result of the high hydrostatic pressure in the precapillaries, an increased amount of aqueous is produced. Aqueous outflow is diminished because of the increased volume of the vessels of the choroid and ciliary processes, which displaces the intraocular contents forward to embarrass the filtration angle.

2. Relation of Glaucoma to Systemic Neurovascular Disease: Several papers have appeared during the past year which indicate a relation of glaucoma to generalized cardiovascular disease and serve as a further argument in support of the neurovascular origin of glaucoma. Sugar,[9] for example, found that 63% of patients

5. (*a*) Kronfeld, P. C., and McGarry, H. I.: Mode of Action of Iris Inclusion Operations, Tr. Am. Ophth. Soc. **48**:107-116, 1950. (*b*) Kronfeld, P. C.: Mechanism of Filtering Operations, Tr. Pacific Coast Oto-Ophth. Soc. **30**:23-40, 1949.

6. Fritz, A.: Blood Circulation and Aqueous Exchange in the Glaucomatous Eye, Bull. Soc. opht. France **96**:58-82, 1951.

7. Kraupa, E.: Glaucoma from the Standpoint of Natural Pathology, Českoslov. oftal. **6**:321-334, 1950.

8. Poos, F.: Genesis of True (Primary) Glaucoma, von Graefes Arch. Ophth. **151**:71-115, 1950.

9. Sugar, H. S.: Etiology of Simple Glaucoma, Proc. XVI Internat. Cong. Ophth., London **2**:846-853, 1950.

with chronic simple glaucoma at the Detroit Receiving Hospital had associated hypertensive vascular diseases and vascular sclerosis. He thinks that the relation was an indirect one, through the process of sclerosis. Such theories, however, cannot explain glaucoma occurring in younger patients with no sclerosis, and they often fail to take cognizance of the fact that glaucoma increases greatly in frequency with advancing age, a time when other degenerative processes, such as vascular disease, also increase in incidence. With this in mind, Sunde [10] compared 100 patients having chronic simple glaucoma with 100 controls and found the incidence of arterial hypertension and other cardiovascular diseases to be equally frequent in the two groups. This was true also of capillary fragility. He concluded, therefore, that there was no relation between the cardiovascular findings and glaucoma.

Matteucci,[11] on the other hand, found evidence to suggest that glaucomatous crises, as well as glaucoma without increased ocular tension, could be associated with systemic arterial hypotension. Benstein [12] found that venous pressure was increased in decompensated glaucoma and offered pressure readings recorded with a needle in the cubital vein to support his hypothesis.

3. Glaucoma and the Cochleovestibular Apparatus: Novel and interesting support for the neurovascular school is offered by observations which relate glaucoma to disturbances in the cochleovestibular function. Cristini and Cristini [13] found definite audiometric disturbances in 18 patients which they suspected were due to an ischemic lesion of the neuroepithelial apparatus, probably much the same as that which occurs in glaucomatous atrophy of the optic nerve. They suggest that the audiometric and the visual-field defects are comparable and that hypacusia may well be an extraocular symptom of glaucoma, occurring on the same vascular basis. Fontana and Cristiani [14] examined 85 patients with Ménière's disease and found that 5 had chronic simple glaucoma. That likewise suggested a common pathogenesis. Godtfredsen [15] suggests that because both primary glaucoma and Ménière's disease respond to dehydration and a low-salt diet, their origins may be similar. He reports three cases in which Ménière's disease and glaucoma were associated. He compares the similar anatomy and the somewhat comparable physiology of the inner ear and the eye. Each has a highly differentiated sensory epithelium enclosed in an inelastic capsule and possesses its own humoral system. Each has a rich blood supply. The aqueous humor, on the one hand, and the endolymph or perilymph, on the other, are secreted and absorbed by a complex mechanism, which

10. Sunde, O. A.: Relationship Between Simple Glaucoma and Other Cardiovascular Diseases, Acta ophth. **29**:213-226, 1950.

11. Matteucci, P.: Glaucoma in Subjects with Arterial Hypotension, Ann. ocul. **183**:313-325, 1950.

12. Benstein, I. Y.: Venous Pressure in Glaucomatous Patients, Vestnik oftal. **29**:21-25, 1950.

13. Cristini, G., and Cristini, W.: Pathologic Nature of Cochlear Hypacusia in Primary Glaucoma, Riv. oto-neuro-oftal. **25**:421-436, 1950.

14. Fontana, G., and Cristiani, M.: Pathogenetic Relations of Ménière's Syndrome and Primary Glaucoma, Riv. oto-neuro-oftal. **25**:341-351, 1950.

15. Godtfredsen, E.: Concurrence of Glaucoma and Ménière's Disease, Acta oto-laryng. **37**:533-538, 1949.

is affected by changes in the blood constituents and the blood volume. This might suggest a common vasomotor disturbance as the cause of disturbances of cochleovestibular function and glaucoma. The relation of these two derangements of function, reported by many critical observers, deserves serious investigation.

4. Disturbances in the Acetylcholine-Cholinesterase Mechanism of the Parasympathetic Nervous System: Disturbances in the acetylcholine-cholinesterase mechanism of the parasympathetic nervous system have been suggested as a possible cause of glaucoma. Elwyn [16] postulates that a deficiency of the normal parasympathetic control over the intraocular pressure results in a deficiency in production of the chemical mediator acetylcholine. He suggests, therefore, that either the constant volume of the aqueous is increased or the constant volume of the blood in the choroidal vessels is increased, or that both are. He adds that early in its course primary glaucoma is strictly functional, but that later, owing to organic changes, such as those of closure of the angle, the condition is organic. He believes that all primary glaucoma represents a single disease, manifest either by an insidious onset and slowly progressive course, as in chronic simple glaucoma, or by an acute onset with rapid rise in ocular tension and the classic signs of acute congestive glaucoma. His evidence is based largely on the fact that drugs which have an acetylcholine-like action or those which inhibit cholinesterase are the ones which are really effective in the treatment of glaucoma.

De Grósz [17] determined the esterase activity of specimens of aqueous from eight eyes with chronic simple glaucoma. Five of the eyes showed an increase of such activity. He recognized that the number of eyes studied was insufficient to warrant final conclusions but believed that his observations might explain the efficacy of miotics in the treatment of primary glaucoma. Filbry,[18] likewise, states that glaucoma may result from a constitutional hypofunction of the parasympathetic nervous system, which becomes manifest later in life, when further hormonal insufficiency of this system occurs.

5. Glaucoma and the Sympathetic Nervous System: Several reports have been submitted advancing the idea that the sympathetic nervous system may be at fault in primary glaucoma. Courtis and Nunez [19] theorize that primary glaucoma is on a basis of hypertonia of the ocular sympathetic nervous system with superimposed excitation of the trigeminus. They state that arteriolar and venous contraction always occur in glaucoma. In chronic glaucoma, the permeability of the capillaries is increased, while in congestive glaucoma there is also capillary dilatation. Niedermeier,[20] in two articles, emphasizes alterations in the function of the autonomic nervous system of the eye as a possible cause of the disease. He found that blood epinephrine was increased in four patients with acute glaucoma and also that it

16. Elwyn, H.: The Problem of Glaucoma, Am. J. Ophth. **33**:1373-1379, 1950.

17. de Grósz, S.: Data Concerning the Pathogenesis of Primary Glaucoma, Ophthalmologica **119**:281-284, 1950.

18. Filbry, E.: Etiology and Pathogenesis of Glaucoma Simplex, Klin. Monatsbl. Augenh. **115**:506-513, 1949.

19. Courtis, B., and Nunez, R. B.: Pathogenesis of Primary Glaucoma, Proc. XVI Internat. Cong. Ophth., London **2**:854-861, 1950.

20. Niedermeier, S.: Regulation of the Intraocular Pressure, von Graefes Arch. Ophth. **150**:665-670, 1950; Glaucoma and the Sympathetic Nervous System, ibid. **150**:385-387, 1950.

became increased after the patients were placed in a dark room. This might signify that the dark-room test for glaucoma exerted its effect through the sympathetic system. Pau [21] found that the ocular tension decreased after systemic administration of ergotamine, which is sympatholytic, and that it was also reduced by sympathectomy. He mentions the frequency with which acute glaucoma is associated with emotional disturbances, in which epinephrine output is known to be increased.

While extremely interesting and difficult to refute, evidence supporting a disturbance in the autonomic nervous system as the underlying factor in glaucoma is as yet inadequate. The above-mentioned arguments, the response of glaucoma to miotics, of which the effective ones are parasympathomimetic, and the tension-lowering effect of dibenamine® (N-N-dibenzl-β-chloroethylamine hydrochloride), which is sympatholytic, however, make the theory very tempting. This is especially true because the mode of action of either group of therapeutic agents is unexplained.

6. Hypothalamic Region: Papers are continuing to appear which suggest that the hypothalamic region of the brain may initiate changes which lead to neurovascular disturbances just mentioned and through them precipitate glaucoma. Among these are articles by Gonzalez-Pola,[22] Schmerl and Steinberg,[23] Rubino and Esente,[24] and Arkin.[25] Schmerl and Steinberg,[23] continuing their previous work, claim to have located, by means of electrical stimulation, two distinct diencephalic centers, controlling pupillary motility and ocular tension. The center for pupillary dilatation, located just anterior to the pituitary gland, when stimulated, caused a reduction of ocular tension. The center for pupillary constriction, located still more anteriorly, when stimulated, caused pupillary contraction and an increase in ocular tension. These observations of Schmerl and Steinberg are particularly interesting because they furnish objective evidence to help in relating the pupillary disturbances associated with glaucoma, described by Lowenstein and Schoenberg, to specific centers thought to control intraocular pressure.

Rubino and Esente,[24] in a study of levels affecting ocular tension, found that hypnotic doses of barbiturates which are known to depress subcortical centers cause a lowering of the retinal arterial and intraocular pressures. Narcotic doses caused the retinal arterial and intraocular pressures to return to normal or beyond. Substances, such as chloral hydrate and ether U. S. P., which inhibit the cortex, caused an elevation of both retinal arterial and intraocular pressure. The authors suggest, therefore, that there is a synergistic mechanism of the cortex and the subcortical centers which is involved in the control of retinal arterial and intraocular pressure.

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21. Pau, H.: Primary Glaucoma Due to Relaxation of Ciliary Muscle as Result of Sympathicotonia, Klin. Monatsbl. **115**:513-524, 1949.

22. Gonzalez-Pola, A. M.: Pathogenesis of True Glaucoma, Arch. Soc. oftal. hispano-am. **10**:592-599, 1950.

23. Schmerl, E., and Steinberg, B.: Separation of the Diencephalic-Centers Concerned with Pupillary Motility and Ocular Tension, Am. J. Ophth. **33**:1379-1381, 1950.

24. Rubino, A., and Esente, I.: Eye and Diencephalon: XII. Behavior of Tonometric Values and Retinal Pressures Under Action of Cortical and Mesodiencephalic Depressors, Riv. oto-neuro-oftal. **25**:351, 1950.

25. Arkin, W.: Influence of Ocular Tension of One Eye on Tension of the Other, Klin. oczna **19**:105-133, 1949.

7. Emotional Disturbances and Glaucoma: The relation of emotional disturbances to attacks of glaucoma is well known and is thought to occur through the neurovegetative centers of the hypothalamus. Enciso [26] states that 73% of cases of glaucoma occur on such a basis. Comments of Ligorio and Toselli [27] upon emotional factors are partially based on a study of the familial incidence of glaucoma. Ripley and Wolff,[28] in a study of 18 patients, found that glaucoma was associated with situations of stress and rarely with happiness.

8. Low-Tension Glaucoma and the Neurovascular Theory: Optic atrophy, cupping of the head of the optic nerve, and visual-field defects characteristic of glaucoma occurring without elevated ocular tension have been used as an argument in favor of the neurovascular origin of glaucoma. Numerous other names have been suggested for the entity, such as pseudoglaucoma, low-tension glaucoma, soft glaucoma, relative glaucoma, and sclerotic atrophy of the optic nerve. In recent years, the subject has evoked lively discussion, partly because of the increasing popularity of the mechanical school of thought. The question has been raised as to whether there is such an entity as low-tension glaucoma. Advocates of the neurovascular school believe that it is the same disease as glaucoma and that the changes in the optic nerve are degenerative or nutritional in origin. They believe that the tension is only incidental and that it is not elevated unless the circulation of the uveal tract is similarly involved.

Blazar and Scheie [29] reviewed the histories of 150 patients with primary glaucoma and found that only a few presented the clinical picture of low-tension glaucoma, or pseudoglaucoma. The tension was consistently normal, and the results of provocative tests were negative. In nearly all cases careful study revealed the etiological factor to be pituitary tumor, congenital coloboma of the optic nerve, syphilitic involvement of the optic nerve, calcification of the internal carotid arteries, or other suspected cause. They conclude that, at least in their experience, low-tension glaucoma is rare and that any patient who presents such a clinical picture should be carefully studied. Even then, if no explanation is found, his condition should be reevaluated periodically. They suggest the term "pseudoglaucoma" for that group of cases in which a definite cause can be found to explain the optic atrophy and visual-field defects, while the term "low-tension glaucoma" should be applied to that group in which no cause is found.

Magitot [30] also assumes that low-tension glaucoma and glaucoma with elevated ocular tension are due to the same underlying neurovascular disease process and uses this reasoning as an argument to support the neurovascular theory. He believes the disturbance to be in the thalamic region. If the uveal circulation is predominantly

26. Enciso, M.: Emotional Glaucoma, Proc. XVI. Internat. Cong. Ophth., London **2**:862-864, 1950.

27. Ligorio, A., and Toselli, C.: Familial Glaucoma in Emotional Subjects, Rass. ital. ottal. **19**:293-300, 1950.

28. Ripley, H. S., and Wolff, H. G.: Life Situations, Emotions and Glaucoma, Psychosom. Med. **12**:215-224, 1950.

29. Blazar, H. A., and Scheie, H. G.: Pseudoglaucoma, Arch. Ophth. **44**:499-513 (Oct.) 1950.

30. Magitot, A.: Basis of the Neuropsychiatric Treatment of Glaucoma, Ann. ocul. **183**:817-828, 1951.

involved, ocular hypertension will result, whereas if the vessels of the retina and optic nerve alone are involved, the picture of low-tension glaucoma will develop. He believes that blockage of the filtration angle is only a secondary, and often an unimportant, change. Meyer [31] conceives of low-tension glaucoma as being incomplete glaucoma and likewise believes that the disease is due to a neurovascular degeneration involving the retina and optic nerve. He thinks that the ocular tension may rise in the later stages of the disease. Werner and MacDougald [32] write that there undoubtedly is a condition in which cupped disks and progressive visual-field changes occur, even though the ocular tension remains normal. They attribute the causative factor to circulatory insufficiency and mention increased venous pressure. Peripheral circulatory disturbances and labyrinthine disturbances are frequently present.

Lemoine,[33] in reviewing the records of 816 patients at the Massachusetts Eye and Ear Infirmary, found that 18, or 2%, had low-tension glaucoma. Provocative tests, however, had not been done. Lloyd,[34] studying 249 eyes, found low-tension glaucoma in 21%.

These diverse opinions as to the true nature of low-tension glaucoma and an incidence reported by critical observers ranging from extremely rare to as high as 21% prove our lack of real knowledge. In many instances preconceived ideas and lack of uniform criteria in diagnosis of the condition help to retard a better understanding of the process. Present statistics are relatively meaningless, and final opinion should be withheld until more revealing information is available.

B. The Mechanical School.—The gonioscopic classification, or the so-called mechanical school of origin, of glaucoma has evolved gradually as a result of the experiences and observations of may persons and has considerable objective evidence to support it. The relation of a shallow anterior chamber to glaucoma has been a known clinical fact since the earliest knowledge of the disease. Raeder [35] made the first histologic correlation of the depth of the anterior chamber and the type of primary glaucoma. Rosengren carried this further when he reported a study of the measurements of the depth of the anterior chamber in eyes with glaucoma, published in 1931. A translation of this classic paper was made available in condensed form in 1950,[36] in the ARCHIVES. He noted that when glaucoma occurred in eyes with a shallow anterior chamber, acute attacks were characteristic. He concluded that the shallow chamber predisposed the eye to these attacks. He found that chronic simple glaucoma can occur in eyes with either a shallow chamber or a chamber of normal depth, a fact that is widely accepted today. The important observations of these two men established the basis for future work by

31. Meyer, S. J.: Incomplete Glaucoma: Monosymptomatic Glaucomatous Excavation, Eye, Ear, Nose & Throat Month. **29**:477-479, 1950.

32. Werner, L., and MacDougald, T. J.: Low-Tension Glaucoma: Its Diagnosis and Treatment, Proc. XVI Internat. Cong. Ophth., London **2**:945-949, 1950.

33. Lemoine, A. N., Jr.: Glaucoma: A Statistical Review of 816 Patients with 1,112 Glaucomatous Eyes, Am. J. Ophth. **33**:1353-1373, 1950.

34. Lloyd, J. P. F.: The Glaucomas: A Survey, Am. J. Ophth. **34**:705-717, 1951.

35. Raeder, J. G.: Untersuchungen über die Lage und Dicke der Linse im menschlichen Auge bei physiologischen und pathologischen Zuständen, nach einer neuen Methode gemessen: II. Die Lage der Linse bei glaukomatösen Zuständen, von Graefes Arch. Ophth. **112**:29, 1931.

36. Rosengren, B.: Studies in Depth of the Anterior Chamber of the Eye in Primary Glaucoma, Arch. Ophth. **44**:523-538 (Oct.) 1950.

Barkan, Gradle, Kronfeld, Sugar, and others, who have elaborated the classification of glaucoma based upon width of the anterior-chamber angle, as determined by gonioscopic studies.

1. Miscellaneous Articles in Support of the Mechanical School: Articles appearing in the literature of this country indicate the growing popularity of gonioscopic concepts. At least three papers appearing during the past year have confirmed the importance of obstruction of the drainage mechanism in glaucoma. Alexander [37] and Lloyd [34] support this concept. Scheie and Frayer [38] and Barkan,[39] working separately, found that air injected into the anterior chamber caused sharp rises in ocular tension. These observers attribute the rise in tension to obstruction of the flow of aqueous from the posterior to the anterior chamber as the consequence of a valve-like action between the anterior surface of the iris and the posterior surface of the air bubble. As a result, aqueous accumulates in the posterior chamber and pushes the periphery of the iris forward around the edge of the air bubble to obstruct completely the angle of the anterior chamber. This was observed by Scheie and Frayer and by Barkan in rabbits and dogs. Both observers found that iridectomy prevented the rise in tension, as did wide pupillary dilatation. Scheie and Frayer produced air glaucoma experimentally in human eyes with a normal anterior segment which were about to be enucleated, and they observed one patient clinically in whom an acute rise in ocular tension was caused by air placed in the anterior chamber. An iridencleisis was necessary to control the tension in this eye, even after evacuation of the air. The signs were identical with those of acute narrow-angle (congestive) glaucoma. There is little doubt that these two papers offer fairly adequate proof of the mechanical origin of at least one type of experimental glaucoma.

Thomassen,[40] in an interesting paper, contributes further evidence of the function of Schlemm's canal. Normal eyes and those with seclusio pupillae were subjected to 25 gm. of pressure for two minutes. The tension fell significantly in normal eyes, but of a series of 10 eyes with seclusio pupillae, the pressure remained normal in 3 and increased in 7. An iridectomy was performed upon two of these eyes and an iris transfixion upon another. After recovery, the tests were repeated, and a normal fall in tension then resulted from the pressure. Thomassen took this to indicate a safety-valve action of Schlemm's canal and assumed that escape of aqueous behind the iris was not a significant factor in the compression phenomenon.

In another paper on the exit of aqueous humor, Thomassen [41] conducted experiments on eyes which had to be removed because of melanoma, but with a normal anterior segment and normal intraocular pressure. A 1% methylene blue solution injected into the anterior chamber prior to enucleation caused staining of some

37. Alexander, G. F.: Causes and Effects of Primary Glaucoma, Tr. Ophth. Soc. U. Kingdom **69**:327-335, 1949.

38. Scheie, H. G., and Frayer, W.: Ocular Hypertension Induced by Air in the Anterior Chamber, Arch. Ophth. **44**:691-702 (Nov.) 1950.

39. Barkan, O.: Glaucoma Induced by Air Blockade, Am. J. Ophth. **34**:567-571, 1951; Glaucoma Induced by Air Blockade: Clinical Observation and Experimental Study, Proc. XVI Internat. Cong. Ophth., London **2**:938-944, 1950.

40. Thomassen, T. L.: The Safety-Valve of the Eye, Acta. ophth. **27**:413-422, 1949.

41. Thomassen, T. L.: On the Exit of Aqueous Humor in Normal Eyes, Acta. ophth. **28**:479, 1950.

epibulbar vessels, but the number increased as the intraocular pressure was raised. When the experiment was repeated after enucleation, the number of stained vessels became so great that they could not be counted. This, he explains, was due to the dye's having easier access to the episcleral veins when they contained no blood, and hence had no opposing pressure. To him, this suggested that the pressure in episcleral veins does not have an effect on regulating the outflow of aqueous. From these observations, he concludes that the eye has a great capacity for compensating for changes in ocular tension. He further theorizes that glaucoma probably resulted from an obstruction to outflow channels. This work might conceivably be used to support either theory of origin of glaucoma.

Grant,[42] using an electronic Schiøtz tonometer equipped with a recording galvanometer, reports a method of measuring both the rate of aqueous-humor formation and the patency of outflow channels. This method presents a means of determining whether or not alterations of steady-state intraocular pressure are due to changes in resistance to outflow or changes in rate of aqueous-humor formation. Such studies should greatly clarify the mechanism of glaucoma. Preliminary studies reported by Grant before the Section on Ophthalmology of the American Medical Association at Atlantic City, on June 14, 1951, to be published in a future issue of the ARCHIVES, tended to confirm the fact that primary glaucoma is due to an obstruction to outflow of aqueous from the eye. He suggested that acute narrow-angle (congestive) glaucoma may be on the basis of an iris-angle block and that wide-angle (chronic simple) glaucoma probably occurs on a different basis. Future reports, using this technique, should reveal much of great interest and importance.

2. Gonioscopic Contributions: The only advance in gonioscopic technique during the past year was the development of a new gonioscopic lens by Troncoso [43]; this instrument is similar to the previous one carrying his name except that it has a hollow tube at its apex, through which the lens can be filled. This facilitates both insertion of the lens and its removal. The Troncoso type of lens is advantageous because if the patient squeezes his lids forcibly the lens is not pushed from the eye, as is the Koeppe type of lens, but, instead, the lids slide over it, causing firmer contact with the globe.

Additional gonioscopic studies have been reported which in general offer support to the mechanical school of origin. Von Fieandt [44] carried out gonioscopic studies upon seven eyes with acute congestive glaucoma and found the angle closed in all. Of 56 eyes with chronic simple glaucoma, half showed a narrow angle, while in the other half the angles were open. These findings tend to confirm existing information.

Hobbs [45] studied the trabeculum of 40 patients with chronic simple glaucoma and was unable to find that it differed in any way from that in a control group

42. Grant, W. M.: Tonographic Method for Measuring the Facility and Rate of Aqueous Flow in Human Eyes, Arch. Ophth. **44**:204-214 (Aug.) 1950.

43. Troncoso, M. U.: Improved Tubular Goniolens for Gonioscopic Examinations, Am. J. Ophth. **34**:282-284, 1951.

44. von Fieandt, A.: Goniocycloscopic Findings in Glaucoma, Cataract and Some Other Pathological Conditions of the Eye, Acta ophth. (Supp.) **34**:1 (Feb.) 1950.

45. Hobbs, H. E.: The Trabecula in Chronic Simple Glaucoma with Special Reference to the Gonioscopic Appearance of Blood in the Canal of Schlemm, Brit. J. Ophth. **34**:489-494, 1950.

of normal eyes. He found that the canal of Schlemm in glaucomatous eyes readily filled with blood, which to him was evidence against sclerosis of the trabeculum. He concludes that his studies fail to confirm the presence of a mechanical block at the angle of the anterior chamber. His data, likewise, can be used to support either argument, because, as pointed out by Kronfeld, normal filling of Schlemm's canal in a glaucomatous eye may only signify trabecular obstruction. In addition, except for exceptional cases, anomalies of the trabeculum which might be used to explain the origin of wide-angle glaucoma, are only rarely demonstrable gonioscopically.

Von Beuningen,[46] on the other hand, in an extensive study of the corneoscleral trabeculum of 273 eyes with primary glaucoma and 250 control eyes, found an increased turbidity of the trabeculum of the glaucomatous eyes, although this cloudiness also increased with age in the control group. Not only did the glaucomatous eyes show the greater turbidity, but the change was most marked in eyes with the high ocular tension. He therefore concludes that increased density in the trabeculum is important in the pathogenesis of glaucoma and offers the theory that it results from sclerosis of the surrounding vessels. Such reasoning may also be used to support both the gonioscopic and the neurovascular school.

3. Aqueous Veins: Greatly increasing interest has been shown in aqueous veins since their original description by Ascher. Numerous observers have confirmed and elaborated upon his work, but the vessels had never been demonstrated anatomically until this year, when Ashton,[47] in a brilliant piece of work, accomplished this purpose. He prepared "neoprene" casts of Schlemm's canal and the vessels with which it communicated in four eyes after enucleation. Six aqueous veins had been identified in these eyes preoperatively by a loop suture. All were of the striated, or laminated, type. Two of the aqueous veins originated directly from Schlemm's canal, while the other four arose indirectly and were connected with it by an anastomosis between the superficial and the deep scleral plexus. Ashton's observations supported Ascher's theory that branches between the superficial and the deep scleral plexus serve as anatomical substrata for many of the aqueous veins. This paper should be read by all ophthalmologists having any interest in glaucoma or the anatomy and physiology of the canal of Schlemm. The chief limitation upon the method is that arteries cannot be distinguished from veins unless previously marked, and filling defects, which are apt to occur, may cause artifacts, which may be misinterpreted. In addition to information yielded regarding aqueous veins, Ashton corroborated much of the work of previous investigators upon Schlemm's canal.

Greaves and Perkins[48] report finding aqueous veins in the eyes of rabbits. Schmerl had previously seen them in rabbit eyes, and Weekers and Prijot, in the eyes of guinea pigs also. Greaves and Perkins found that increased pressure on the globe caused a marked increase in flow of the clear fluid within the aqueous veins. Artificial elevation of the intraocular pressure by a needle connected to a

46. von Beuningen, E. G. A.: Optical Density of the Corneoscleral Trabeculum in Primary Glaucoma, Ber. Versamml. deutsch. ophth. Gesellsch. **56**:132, 1950.

47. Ashton, N.: Anatomical Study of Schlemm's Canal and Aqueous Veins by Means of Neoprene Casts: I. Aqueous Veins, Brit. J. Ophth. **35**:291-303, 1951.

48. Greaves, D. P., and Perkins, E. S.: Aqueous Veins in Rabbits, Brit. J. Ophth. **35**:119-123, 1951.

manometer containing saline did likewise. India ink, when injected into the anterior chamber, did not appear in the aqueous veins, but Evans blue did so very rapidly. This suggested the presence of a structure between the anterior chamber and the aqueous veins which does not permit the passage of particles over 1 μ in size. Flow in the aqueous veins also increased upon irritation of the iris. Stimulation of the cervical sympathetic fibers with small amounts of electricity caused an increase in flow through these vessels, while greater stimulation initially caused an increased flow but later produced such extreme contraction of all the limbal vessels that the entire region appeared avascular. This article is significant because it indicates a barrier between the anterior chamber and the aqueous veins, either the trabeculum or the canal of Schlemm or both. It also seems of significance that with increased pressure, and presumably no change in this barrier, increased amounts of aqueous flowed through the aqueous vessels. This occurred either when the ocular tension was experimentally raised by injecting saline into the anterior chamber or when pressure was applied externally. The clinical implications of aqueous veins in the human eye as yet remain in the realm of conjecture, but the anatomical studies of Ashton and increasing knowledge regarding their physiology lend support to their importance. A summary of the possibilities was presented by Scheie when he reviewed the opinions of Ascher, Goldmann, Gaba, Thomassen, and Weinstein. As pointed out in that review, information now available on aqueous veins can be used for or against either the mechanical or the neurovascular theory.

Other reports pertaining to aqueous veins include one by Huggert,[49] who reports that after corneal abrasions fluorescein penetrates the anterior chamber, enters the aqueous veins, and renders them visible. He concludes that this phenomenon, observed in 15 patients, was further proof that aqueous veins contain aqueous. Kleinert and Grün [50] note that when pressure is applied to the eye, blood flows back from the episcleral veins into the aqueous veins at a critical point, which he terms "the compensation maximum." In cases of glaucoma, this reversal of flow occurs when 100 gm. or less is applied to the globe, whereas in normal eyes reversal does not occur until the pressure applied reaches 150 gm. or over. They believe that aqueous, modified under pressure, causes swelling of the collagenous fibers of the trabeculum, producing increased resistance to filtration. This blockage occurs at lower pressure levels in glaucomatous eyes. Linnér, Rickenbach, and Werner [51] report further studies on pressure within the aqueous veins, as compared with pressure in the conjunctival veins in normal eyes. Both Goldmann and Linnér had previously found that the pressure in the aqueous veins was about equal to that in the canal of Schlemm, but the readings obtained by Linnér were higher than those of Goldmann. Linnér had used a pressure chamber connected to a water manometer, while Goldmann had used a torsion balance. Linnér, Rickenbach, and Werner, therefore, repeated these studies, using both methods, and found that when a pressure chamber was used the pressure in the aqueous veins was slightly lower than that in the conjunctival veins with the patient in the sitting position. The

49. Huggert, A.: Further Support to the Hypothesis That Ascher's Aqueous Veins Contain Aqueous Humor, Acta ophth. **27**:119, 1949.

50. Kleinert, H., and Grün, P.: The Compensation Maximum, a Glaucoma Symptom, Klin. Monatsbl. Augenh. **118**:449-468, 1951.

51. Linnér, E.; Rickenbach, C., and Werner, H.: Comparative Measurements of Pressure in the Aqueous Veins and Conjunctival Veins, Acta ophth. **28**:469, 1950.

pressure in both vessels was slightly higher when the patient was reclining. They found that the pressures, although comparable, were higher when recorded with the torsion balance. They conclude that the difference obtained between the two methods is significant and that further investigation will be necessary to determine the pressure gradients within the aqueous and the conjunctival veins.

Rickenbach and Werner,[52] in another study, reported a tendency toward lower pressure in the aqueous veins of eyes with high ocular tensions, a finding which also might suggest an obstruction between the anterior chamber and the aqueous-outflow mechanism. Weekers and Prijot [53] found that the application of epinephrine to the conjunctiva caused a constriction of all aqueous veins and thereby increased the resistance to outflow, giving a slight increase in ocular tension. They state that this increase was not in proportion to the amount of constriction, a fact which could probably be explained by anastomoses between Schlemm's canal and the venous network of the anterior segment of the eye. Weekers and Delmarcelle [54] report finding in a corneal leukoma aqueous veins which showed all the characteristics of aqueous vessels.

4. Miscellaneous Articles: Numerous papers continue to appear suggesting causes of glaucoma, all of which theories are unconfirmed. François, Deweer, and van den Berghe [55] report an excellent study on the effect of heredity, particularly in congenital, juvenile, or acute congestive glaucoma, the importance of which is recognized by most ophthalmologists. The familial tendency to glaucoma is well known, but all would agree that, except in occasional cases, heredity probably is not the sole cause. Papers by Godtfredsen,[56] Klar,[57] and Haselmann [58] all report studies attempting to correlate liver disease with glaucoma. Reports by these authors all fail to support any such theory. The possibility of a hormonal disturbance as a cause of glaucoma was raised in several papers. Radnót and Csillag,[59] and de Grósz [60] reported no findings of positive significance, whereas Obal [61] observed that patients predisposed to glaucoma showed rises in ocular tension after the

52. Rickenbach, K., and Werner, H.: Relationship of Apparent Outflow Pressure, Ocular Tension and Pressure in the Aqueous Veins, Ophthalmologica **120**:22-27, 1950.

53. Weekers, R., and Prijot, E.: Vasoconstriction of Aqueous Veins and Relation to Intraocular Pressure, Ophthalmologica **121**:264-272, 1951.

54. Weekers, R., and Delmarcelle, Y.: New-Formed Aqueous and Laminated Veins in a Corneal Leukoma, Acta ophth. **29**:85-89, 1951.

55. François, J.; Deweer, J. P., and van den Berghe: Simple Chronic Glaucoma as a Hereditary Dominant, Bull. Soc. belge d'opht. **96**:665-683, 1950.

56. Godtfredsen, E.: Glaucoma and Liver Function, Acta med. scandinav. **136**:130-135, 1949.

57. Klar, R.: Question of Glaucoma and Hepatic Pathology, Together with Investigations of Intraocular Pressure in Liver Diseases, Klin. Monatsbl. Augenh. **116**:600-614, 1950.

58. Haselmann, G.: Researches on Glaucoma and General Diseases; Klin. Monatsbl. Augenh. **115**:527-534, 1949; Hepatic Function Studies in Primary Glaucoma, ibid. **116**:596-600, 1950.

59. Radnót, M., and Csillag, M.: Hormone Excretion of Glaucomatous Patients, Ophthalmologica **118**:998-1002, 1949.

60. de Grósz, S.: Hormone Excretion of Glaucomatous Patients: Comments on the Paper of M. Radnót and M. Csillag,[59] Ophthalmologica **120**:400, 1950.

61. Obal, A.: (*a*) Increase of Intraocular Pressure Caused by Follicular Hormone, Klin. Monatsbl. Augenh. **116**:418, 1950; (*b*) Hormonal Regulation of Ocular Tension, Ber. Versamml. deutsch. ophth. Gesellsch. **56**:136-146, 1950.

administration of depot follicular hormone or testosterone propionate. Follicular hormone caused the greatest rise. Von Hofe [62] reported 12 cases of inflammatory glaucoma in patients with a febrile illness, probably coincidental.

C. General Comment.—The wide range of opinions expressed in the literature of the past year regarding the mechanism of glaucoma indicates the interest in this vital phase of ophthalmology and serves, also, to underscore our lack of knowledge on the subject. Conclusive objective evidence is lacking for both the neurovascular and the mechanical theory. Even though the arguments of the mechanical school are accepted, and much reliable objective evidence can be found in their favor, the effect of emotional factors, heredity, hormonal balance, autonomic disturbances, and even other factors, cannot be denied. Final judgment should, therefore, be withheld until the results of many more studies are available. It seems most likely that primary glaucoma will be separated into several entities, in some of which one factor predominates, while in others still different factors are at fault.

II. Diagnosis

A. General Considerations.—The diagnosis of glaucoma presents, from a practical point of view, one of the most important problems in clinical ophthalmology, because effective treatment depends to a great extent upon early recognition of the disease. Little of an original nature has been contributed during the past year, although much is being done by way of education through the National Society for the Prevention of Blindness, our medical schools, and ophthalmology in general. Fralick,[63] in a recent symposium on secondary glaucoma, emphasized the need for periodic examination of the eyes by a competent ophthalmologist in patients over 40 years of age. He estimated that some 800,000 Americans now have glaucoma but do not know it, and that glaucoma was responsible for the 22,000 new cases of blindness in the United States in 1950.

One of the important developments in this country during recent years, of aid in both diagnosis and treatment, is the setting up of glaucoma clinics in the various departments of ophthalmology. The importance of such a program in the management of glaucoma is evidenced by the growth of such clinics not only here but in foreign countries. MacIndoe and Shortridge [64] mention the establishment of such clinics in Sydney, Australia, and in Hobart, Tasmania.

The diagnosis of glaucoma continues to be made by suspecting every eye of its presence and carrying out a careful examination of the eye, as well as accurate tonometric studies, painstaking visual-field determinations, and provocative tests.

B. Tonometry.—Friedenwald [65] again emphasizes the importance of recording tonometric readings with two different weights, to rule out discrepancies in ocular rigidity which might interfere with accuracy of determinations. If the two readings are in close approximation, they can be accepted as valid and the ocular rigidity assumed to be within normal limits. If the reading in millimeters of mercury with

62. von Hofe, K.: Clinical Observations on Glaucoma Complicating General Diseases, Ber. Versamml. deutsch. ophth. Gesellsch. **55**:179-181, 1949.

63. Fralick, F. B.: Symposium on Secondary Glaucoma, Am. J. Ophth. **33**:16-65, 1950.

64. MacIndoe, N. M., and Shortridge, D.: First Impression of a Glaucoma Clinic, Tr. Ophth. Soc. Australia **9**:23-24, 1949.

65. Friedenwald, J. S.: Some Problems in the Diagnosis and Treatment of Glaucoma, Am. J. Ophth. **33**:1523-1538, 1950.

the heavier weight is lower than that with the lighter weight, scleral rigidity is low, and intraocular pressure is higher than recorded. If, however, the reading in millimeters of mercury with the heavy weight is considerably higher than that with the lighter weight, ocular rigidity is high, and intraocular tension is lower than recorded. Posner [66] emphasizes the same point. Posner [67] reviews the recent developments of tonometry, mentioning the Harrington tonometer, the Mueller electric tonometer, and the improved Sklar-Schiøtz tonometer. He also discusses the new Berens-Tolman tonometer, which records whether the ocular tension is above or below a previously determined level, for example, 25 mm. Hg. This instrument was constructed primarily for the general practitioner and possesses the advantages of low cost and simplicity in its operation.

C. Perimetry.—Perimetry not only is of extreme importance in the diagnosis of glaucoma but also is the most accurate method of following the clinical course of the disease and aids somewhat in the prognosis, a point emphasized by Posner and Schlossman.[68] According to them, the sudden appearance of an arcuate scotoma in a previously normal half-field, when the first half has already been lost, is a much graver prognostic sign than the mere presence of moderately increased ocular tension.

As an aid to diagnosis, Blaxter [69] studied enlargement of the blind spot in 35 cases of glaucoma and found scotomas which could be demonstrated only with small objects in 15. Except for baring of the blind spot, the scotomas were found in the temporal field, most frequently the upper, about 15 to 25 degrees from the fixation point. These became connected with the blind spot. Even then, a denser nucleus could be found within the scotoma, at a distance from the blind spot, corresponding to the original defect. He made the point that enlargement of the blind spot is an inaccurate term, which had already been given by Traquair.

Castagno [70] analyzed three cases of chronic simple glaucoma and found that the smoking of one cigaret could produce rather marked enlargement of the angioscotoma. The tests were made after a period of abstention from tobacco. On this basis, he stated that it would be advisable to have patients with glaucoma who are sensitive to nicotine stop smoking. Further studies will have to be made on a greater number of patients before any definite conclusions can be drawn, for the author studied only three.

D. Provocative Tests.—Bietti [71] describes a new provocative test which consists of compressing the eye for 10 minutes with a dynamometer sufficiently to elevate the intraocular pressure to levels higher than the diastolic pressure of the central

66. Posner, A.: Role of Ocular Rigidity in Tonometry, Eye, Ear, Nose & Throat Monthly **29**:321-322, 1950.

67. Posner, A.: Recent Developments in Tonometry, Am. J. Ophth. **34**:865-870, 1951.

68. Posner, A., and Schlossman, A.: The Visual Field as an Aid to Prognosis, Am. J. Ophth. **33**:1391-1397, 1950.

69. Blaxter, P. L.: A Note of the So-Called Enlargement of the Blind Spot in Glaucoma, Brit. J. Ophth. **34**:404-406, 1950.

70. Castagno, M. M.: Clinical Observations of the Effect of Tobacco on the Angioscotoma in Glaucoma, Am. J. Ophth. **33**:1431-1433, 1950.

71. Bietti, G.: A New Provocative Test for the Early Diagnosis of Chronic Glaucoma: Behavior of the Blind Spot Under Experimental Dynamometric Compression of the Eye, Proc. XVI Internat. Cong. Ophth., London **2**:895-907, 1950.

retinal artery, but not above systolic pressure. In normal subjects, only a small enlargement of the blind spot occurred to small white test objects. Patients having early chronic simple glaucoma had a more pronounced enlargement of the blind spot. With discontinuation of the compression, the size of the blind spot in healthy eyes rapidly returned to normal. In glaucomatous eyes, secondary enlargement of the blind spot generally occurred after 10 to 15 minutes, which period corresponded to the secondary rise in tension that is seen in glaucomatous eyes after compression.

Gonzalez-Pola,[22] in an interesting paper, emphasizes the value of studying the effect of vasodilators, such as nicotinic acid, injected intravenously upon ocular tension, for he claims that dilatation of the intraocular vessels produces increased capillary permeability, with greater aqueous flow and consequent elevation of tension. He emphasizes the importance of the role of intraocular circulation in the production and drainage of aqueous.

Schmidt,[72] in a review of the various provocative tests used in the diagnosis of glaucoma, finds that the water test is the most reliable. However, if the result is negative, he advises use of the caffeine or the homatropine test. Weinstein,[73] in an excellent paper, reports his evaluation of recent provocative tests for glaucoma. He found that injections of an extract of the posterior lobe of the pituitary ("exophysin," "pituisan," "glanduitrin") rendered the water-provocative test more sensitive and that smoking of cigarets likewise increased the sensitivity of the test. The antidiuretic effect of the hormone and of nicotine apparently increases water retention. Weinstein states that the water-provocative test, combined with hormone injection and smoking, is applicable to all types of primary glaucoma.

In an attempt to determine whether the water-drinking test depends upon the function of the capillary endothelium or osmotic changes in the blood, Leydhecker [74] performed 168 tests, using 250 to 1,000 cc. of water, on 42 patients with primary glaucoma. He found that the test gave positive results with equal frequency in chronic simple and in congestive glaucoma. By studies of the electrical resistance of the blood serum, he showed that the conductivity was decreased, and he arrived at the conclusion that osmotic changes in the blood explained the rise in tension occurring in the water-drinking test. In further studies, he [75] showed that in 16 cases of bilateral glaucoma the permeability of the blood-aqueous barrier to fluorescein did not depend significantly on whether the tension rose after the ingestion of water or whether the injection of fluorescein was made immediately or 15 minutes after the ingestion.

In a third paper on provocative tests, Leydhecker [76] compares results obtained by the venous congestion, or cuff, test, the cold pressor test, and the lability test in both normal and glaucomatous eyes. All these tests act through the vascular system of the eye. Venous congestion was produced with the sphygmometer around

72. Schmidt, K.: Tolerance of the Glaucomatous Eye in Diagnosis and Therapy, Klin. Monatsbl. Augenh. **116**:614-627, 1950.

73. Weinstein, P.: Evaluation of Recent Provocative Tests for Preglaucoma, Am. J. Ophth. **33**:1442-1444, 1950.

74. Leydhecker, W.: The Water-Drinking Test, Brit. J. Ophth. **34**:457-479, 1950.

75. Leydhecker, W.: Permeability of the Blood-Aqueous Barrier to Fluorescein During the Water-Drinking Test in Glaucomatous Eyes, Brit. J. Ophth. **34**:480-483, 1950.

76. Leydhecker, W.: Comparative Provocative Tests in Glaucoma, Brit. J. Ophth. **34**:535-544, 1950.

the patient's neck, inflated to 40 or 45 mm. Hg for one minute. The cold pressor test was carried out by having the subject immerse one hand up to the wrist in a bowl of ice water for one minute. When the two tests were done simultaneously, he termed them the lability test. He also compared the effects of all three tests with the results of water-provocative tests, consisting of the ingestion of 500 to 1,000 cc. of water before breakfast. The rise in tension caused by the lability test was not equal to that brought about separately by the cuff test or the ice test. He concludes that it offers no clinical advantages over the cuff test alone. On comparing the results of the water-provocative test with those of the lability test in a group of glaucomatous eyes, he found that the water-provocative test was the more dependable.

Powell [77] reports a fatality due to cardiac failure, precipitated by a water-provocative test followed by a cold pressor test with a blood pressure cuff about the neck. He therefore urges caution, particularly in the use of the cold pressor test in the presence of cardiovascular disease, hypertension, or other severe systemic disease. In the reviewer's opinion, considerable caution should also be used in employing the water-provocative test, particularly with older people, because of the temporary increase in blood volume which is produced.

III. Medical Treatment of Glaucoma

No startling advances have been made in the medical treatment of glaucoma during the past year. Most of the articles published represent further evaluations of previously known methods of therapy. Several excellent review articles have been published. That by Adler [78] lucidly presents the medical treatment of glaucoma, as advocated by adherents to gonioscopic concepts. He briefly emphasizes early diagnosis, presents the reasons for subdividing glaucoma into the wide- and the narrow-angle type and discusses the therapeutic regimen for each. A thorough trial of miotics is advocated for wide-angle glaucoma, whereas early operation is urged for patients with the narrow-angle type. McGuire [79] briefly reviews the treatment of glaucoma from the standpoint of the general practitioner. He likewise follows principles advocated by the gonioscopic school. However, in the same article, he accepts the theory that progressive field changes in well-controlled glaucoma are probably a result of vascular disease. Gallois,[80] on the other hand, reviews the medical treatment of glaucoma from the neurovascular point of view, to a large extent on the basis of his own experiences. Kravitz [81] emphasizes the importance of the glaucoma problem and advocates the establishment of glaucoma clinics. He reviews the effects of the various types of miotic treatment and is enthusiastic about the use of carbachol U. S. P. (carcholin®).

A. Miotics.—1. Diisopropyl Fluorophosphate (DFP): Several articles, which as a whole are enthusiastic, have presented results obtained with the use of

77. Powell, L. S., Jr.: Fatality Precipitated by Provocative Test for Glaucoma, Kresge Eye Inst. Bull. **2**:19-20, 1950.

78. Adler, F. H.: Treatment of Glaucoma, Postgrad. Med. **7**:95-99, 1950.

79. McGuire, W. P.: Management of Primary Glaucoma, Virginia M. Month. **77**:351-360, 1950.

80. Gallois, J.: Medical Studies on Chronic Glaucoma, Presse méd. **58**:1399-1400, 1950.

81. Kravitz, D.: Glaucoma: Some Social and Medical Aspects, Am. J. Ophth. **33**:1381-1387, 1950.

diisopropyl fluorophosphate in the treatment of glaucoma. Kravitz [81] states that he was rather disappointed in its use but urges that it be given a trial in all cases of glaucoma that have not responded to other miotics. Böck and Veitl,[82] although having treated a limited number of patients, believe that the drug is of considerable help in the management of glaucoma. They state, as had Leopold and Comroe previously, that it is especially effective in counteracting pupillary dilation from atropine. Bond [83] states that diisopropyl fluorophosphate is the drug of choice in aphakic glaucoma, and he found it to be effective in 10 of 27 eyes with chronic simple glaucoma. In five of these eyes the disease had been uncontrolled by previous miotic therapy. Ferrer [84] treated 17 patients with chronic glaucoma for periods of from 4 months to 1½ years. Ciliary spasm occurred in four patients, necessitating discontinuation of the drug with one. The tension was controlled in the rest of patients, and visual-field changes did not progress. The use of diisopropyl fluorophosphate was urged for all patients with glaucoma when surgery is contraindicated. Hauck and Biggins [85] treated 12 patients whose glaucoma was refractive to other types of therapy, and all benefited by its use. In two instances, pilocarpine was effective after the use of diisopropyl fluorophosphate, although it previously had been ineffective.

2. Tetraethylpyrophosphate: Grant [86] reports having treated a series of 60 patients with glaucoma by means of tetraethylpyrophosphate, whose intraocular pressure previously had been unsatisfactorily controlled by pilocarpine or physostigmine. When effective, its administration was continued, but therapy was interrupted from time to time for the trial of other miotics. Treatment was carried out in this manner because it was felt that a miotic, to achieve a place in therapeutics, should prove distinctly better than other available drugs. In accordance with this policy, tetraethylpyrophosphate was gradually discontinued in all but 2 of the 60 cases during a 1½-year period after the beginning of therapy. In approximately one-half the cases the tetraethylpyrophosphate was discontinued within the first two months of therapy, for various reasons. It failed to control the tension, even at the outset, in 14 cases. In another group, of 11 cases, although the treatment was successful initially, the tension again became elevated after periods of 2 weeks to 1½ years. In 16 cases, after a trial period with tetraethylpyrophosphate of one to nine months, equally good control was found with other miotics, such as diisopropyl fluorophosphate or with increased doses of pilocarpine, or physostigmine plus methacholine (mecholyl®), or some other drug. Local allergic reactions occurred in six cases, coming on within two weeks to six months after the beginning of therapy. Inability to tolerate the drug because of blurring of vision from spasm of accommodation prevented further use in two cases, but Grant found that tetraethylpyrophosphate

82. Böck, J., and Veitl, W.: Experiences with Diisopropyl Fluorophosphate (DFP) in Normal and in Glaucomatous Eyes, Ber. Versamml. deutsch. ophth. Gesellsch. **55**:185-191, 1949.

83. Bond, F. M.: Di-Isopropyl Fluorophosphate in Glaucoma, Tr. Pacific Coast Oto-Ophth. Soc. **30**:115-120, 1949.

84. Ferrer, O.: Results in a Series of Cases Treated with Diisopropyl Fluorophosphate, Ophth. ibero am. **12**:123-124, 1950.

85. Hauck, D. L., and Biggins, C. H.: Use of DFP in Treatment of Refractory Glaucoma, M. Arts & Sciences **3**:53-55, 1949.

86. Grant, W. M.: Additional Experiences with Tetraethyl Prophosphate in Treatment of Glaucoma, Arch. Ophth. **44**:362-364 (Sept.) 1950.

was more easily regulated with regard to the patient's comfort than was diisopropyl fluorophosphate, probably because of its shorter action. Except for the shorter action, Grant concluded that there is no fundamental difference between these two drugs in their effectiveness in controlling pressure. Likewise, there is no difference in toxicity except for the sensitization phenomenon.

Tetraethylpyrophosphate and diisopropyl fluorophosphate both have the disadvantage of being decomposed by water, even in small amounts. Grant found that in several instances failure to control pressure resulted from destruction of the drug through contamination of the solution with water, possibly through transfer of tears by the medicine dropper or by washing the dropper with water. The presence of water should be suspected when oily solutions of these miotics present a milky or turbid appearance, due to emulsification of the water droplets. This important observation is worthy of emphasis. Grant concludes his article by stating that tetraethylpyrophosphate offers no distinct advantage over other strong miotics and, in addition, possesses the disadvantage of causing local sensitization in a considerable number of instances.

3. Furthrethonium (Furmethide®): During the past year, after a survey of ophthalmologists, Smith, Kline & French Laboratories removed furthrethonium (furmethide®) from the market because of its irritative nature. Within a few months after the initiation of treatment many patients show tearing, mild itching, hyperemia, and thickening of the conjunctiva. In some patients obstruction of the nasolacrimal apparatus develops, as first reported by Shaffer and Ridgway,[87] in an excellent paper. These authors state that of 21 patients using furthrethonium for three months or longer, 15, or 71%, had tearing within 3 to 12 months. Of the 15 patients with tearing, 12, or 80%, had demonstrable occlusion of the tear ducts, located anywhere from the punctum through the nasolacrimal duct. Conjunctival scrapings revealed nonspecific chronic inflammation. There were no eosinophils, keratinization, or bacteria. Several biopsies showed only nonspecific acute and chronic inflammation.

4. "Mintacol": "Mintacol" (diethoxyphosphor acid-*p*-nitrophenol ester), a new synthetic miotic agent used in the treatment of glaucoma, has been the subject of several articles in the German literature. It is stable in aqueous solution but is rapidly destroyed in an alkaline medium or at temperatures above 50 C. It is effective, as are physostigmine and diisopropyl fluorophosphate, through the inhibition of choline esterase. It is used in aqueous solutions in strengths of 1:6,000, or in oily solutions in strengths of 1:5,000 when slow absorption is desired.

Huerkamp and Wagner[88] found that miosis began in about 11 minutes and persisted from 3 to 10 days. In normal eyes the tension was lowered slightly. "Mintacol" temporarily contracted an atropine-dilated pupil, but unless more of the drug was given, mydriasis recurred. The authors observed its use in 200 cases of chronic simple glaucoma and found it to be at least as good as, and probably better than, pilocarpine and physostigmine. It was used in 31 cases of acute glaucoma and controlled the tension in every instance, but in many eyes a secondary

87. Shaffer, R. N., and Ridgway, W. L.: Furmethide Iodide in Production of Dacryostenosis, Am. J. Ophth. **34**:718-720, 1951.

88. Huerkamp, B., and Wagner, O.: Effect of "Mintacol" on the Pupil and the Intraocular Pressure, Klin. Monatsbl. Augenh. **117**:586-597, 1950.

rise occurred after one or two days. Of the 31 eyes, all but 2 had eventually to be operated upon. Discomfort from ciliary spasm was not excessive. Neuenschwander [89] reports the use of "mintacol" in 40 cases of glaucoma, in 5 of which the disease could not be controlled by other miotics. "Mintacol" was successful in all. He is extremely enthusiastic about its use, finding that it is well tolerated and that two or three daily administrations are generally sufficient. Wirth [90] also gives a favorable report on its use.

B. Sympatholytic Drugs.—1. Dibenamine®: Further information regarding the use of dibenamine® in the treatment of glaucoma is accumulating in the literature. The drug was originally introduced for this purpose by Christensen and Swan, in 1948. An excellent study was carried out by Newell, Ridgway, and Zeller [91] to determine its effect after intravenous injection. They found that constriction of the pupil was the earliest sign of the action of dibenamine® in normal eyes and that it was particularly marked in persons who had been receiving a miotic. It was most pronounced in man and the cat but did not occur in the rabbit or guinea pig. Ptosis is only slight and not constant. Enophthalmos was not observed. Visual acuity was unaffected. The intraocular pressure falls 5 to 10 mm. Hg, with the hypotension persisting less than 24 hours. No change was observed in the blood vessels of the fundus or the conjunctiva.

The authors employed dibenamine® for the treatment of various types of glaucoma which did not respond to the usual medical measures. Absolute glaucoma responded poorly. In cases of secondary glaucoma the average fall in ocular tension was 26.2 mm. Hg. However, the drug was useful in only one of seven patients with this type. Two patients with acute narrow-angle glaucoma derived the greatest benefit from dibenamine,® the tension falling to levels safe for surgical intervention. Patients with this form of glaucoma responded more promptly than patients with other types of glaucoma. The lowest pressure occurred at an average of two hours after administration of the drug.

The authors conclude that, since the drug was effective in atropinized eyes, its action could not have been due to enhancement of cholinergic innervation by blocking the antagonistic adrenergic innervation. They believe that the tension-lowering effect was independent of changes in the angle of the anterior chamber caused by action on the dilator pupillae. Since the drug was effective in cases of iris bombé, its action could not have been limited to the anterior segment but must be either on the posterior segment exclusively or on both. Its hypotensive effect, also, was not due to variations in the arterial blood pressure, which were only slight, and the authors do not believe that it was due to the effect upon the epinephrine-sensitive secretory activity of the ciliary body, at least in the rabbit and guinea pig. They found that the greatest objection to dibenamine® was its transient effect. The intraocular pressure began to rise long before the systemic effects had disappeared, precluding further administration of the drug during the period of maximum reduction of tension.

89. Neuenschwander, M.: Mintacol (Bayer), a New Glaucoma Drug, Ophthalmologica **120**:104-105, 1950.

90. Wirth, W.: Pharmacology of a New Synthetic Drug, "Mintacol," for Glaucoma, Deutsche med. Wchnschr. **74**:1243-1245, 1949.

91. Newell, F. W.; Ridgway, W. L., and Zeller, R. W.: Treatment of Glaucoma with Dibenamine, Am. J. Ophth. **34**:527-535, 1951.

Clark and Duggan [92] describe their experiences in the treatment of glaucoma with dibenamine® in 10 cases of acute congestive glaucoma and in 1 of chronic simple glaucoma. In 7 of the 10 cases, the ocular tension was reduced to normal, or almost normal, after the administration of dibenamine.® In the other three cases, although the tension did not return to normal, there was an appreciable reduction. However, in all instances in which further therapy was not instituted, the intraocular pressure began to rise, and the symptoms returned as soon as the blocking action of dibenamine® wore off. Toxic reactions appeared in 5 of the 11 cases. These included nausea, with or without vomiting; headaches; increased pain in the affected eye; a sensation of chilliness; pain at the site of the injection and along the vein; mental confusion; visual hallucinations, and light coma, with twitching of the muscles of the face and neck. The one instance of coma and muscle twitching occurred in a diabetic patient. The authors suggest that dibenamine® may exert its effect by relieving spasm of the uveal vessels, with improvement in circulation of the uveal tract, a concept in line with the trend of thought that acute congestive glaucoma may result from a circulatory disturbance. The authors conclude that dibenamine® seems to have a place in the treatment of glaucoma chiefly as a means of reducing the intraocular pressure prior to surgery, although they mention a disturbingly high incidence of toxic reactions.

2. Miscellaneous Sympatholytic Drugs: Stocker [93] reports experiences with the use of four compounds—tetraethylammonium chloride (etamon® chloride), priscol® (2-benzyl-4,5-imidazoline hydrochloride), compound 7337 (Ciba), and compound 501 (Smith, Kline & French), all of which inactivate the sympathetic nervous system. He believes that drugs 7337 and 501 showed the most consistent results in reducing the intraocular pressure in rabbits when given intravenously. His impression is that compound 7337 is a useful drug in the treatment of certain forms of glaucoma without definite blockage of the chamber angle. He believes that these drugs will be effective only in those types of glaucoma in which a derangement of the autonomic nervous system plays a part in the elevated ocular tension.

Posner [94] studied the effect of certain hydrogenated alkaloids of ergot on glaucoma. The drugs used were dihydroergocornine, dihydroergocristine, and dihydroergokryptine. He states that the pharmacodynamic action of the hydrogenated alkaloids of ergot is characterized by a complicated interplay of central and peripheral mechanisms. The peripheral phase is one of adrenergic blockage, while the nature of the central mechanism is less well known but becomes manifest therapeutically by a depression of tone, mainly arteriolar, in the various vascular beds. As a result, the systemic blood pressure decreases, and peripheral blood flow increases. The hydrogenated alkaloids differ fundamentally from the parent alkaloids in that they have no uterotonic or vasoconstrictor action and exhibit more powerful adrenergic-blocking activity. The drugs were administered to 29

92. Clark, W. B., and Duggan, J. W.: Use of Dibenamine in Treatment of Acute Congestive Glaucoma, Am. J. Ophth. **34**:535-542, 1951.

93. Stocker, F. W.: Systemic Use of Newer Sympatholytics and Parasympathetic Stimulants for Influencing the Intraocular Pressure, Proc. XVI Internat. Cong. Ophth., London **2**:916-927, 1950.

94. Posner, A.: Effect of Certain Hydrogenated Alkaloids of Ergot on Glaucoma, Am. J. Ophth. **33**:1551-1554, 1950.

patients—17 with chronic simple glaucoma and 12 with acute congestive glaucoma. In patients with chronic simple glaucoma, the tension was not lowered, nor was any other demonstrable effect noticed in the eye. In acute congestive glaucoma, regardless of the cause, the intravenous administration of the drug resulted in almost immediate relief of pain and lowering of the ocular tension by an average of 30%. A mixture of the three substances was somewhat more effective than any one of them given singly. The first two administrations are usually more efficacious than subsequent ones. The drugs may be administered at intervals as short as four hours, but usually one or two injections suffice to control pain. Posner suggests, as have others, that this type of substance be used to control pain and to lower tension preparatory to surgical procedures.

Another report on the use of ergot alkaloids was submitted by Rintelen and Smolik,[95] who employed a mixture of equal amounts of three hydrogenated alkaloids of the ergotoxin group, called hydergin, with equivocal results. The action and effectiveness of these drugs, as judged by these reports, seem comparable to those of dibenamine.*

C. Miscellaneous Therapy.—1. Vitamins: Reports of other miscellaneous therapeutic approaches to glaucoma, some extremely novel, have appeared during the past year. Niedermeier [96] found that 10% thiamine hydrochloride increased the miotic and tension-lowering properties of methacholine or pilocarpine when given locally. Ferrante and Rossetti [97] observed the same phenomenon with thiamine after the use of 50 to 100 mg. intravenously in cases of acute glaucoma. They attributed this to the anticholinesterase activity of the vitamin.

2. Hormones: Obal,[98] on the basis of having observed a rise in tension following the use of follicular hormone, treated several patients having glaucoma with its antagonist, progesterone, the corpus luteum hormone. He found that the tension fell in a significant number of patients, and even when the tension was not lowered the symptoms abated. His observations are extremely interesting and should be subjected to further trial. He suggests that injections of follicular hormone might be valuable as a provocative test.

Blake and associates [99] used corticotropin (ACTH) in the treatment of primary glaucoma, without effect. Since they found that it was useful in the treatment of secondary glaucoma due to uveitis, they believe that the drug might be used as a differential diagnostic test.

3. Psychotherapy: Magitot [80] emphasizes the general management of the patient, particularly from the psychiatric point of view, as did Ripley and Wolff.[28]

95. Rintelen, F., and Smolik, H.: Effect of Hydergin upon the Intraocular and Diastolic Retinal Arterial Pressure, Ophthalmologica **120**:100-103, 1950.

96. Niedermeier, S.: Experimental Studies of the Mechanism Regulating the Ocular Tension, Ber. Versamml. deutsch. ophth. Gesellsch. **56**:134-136, 1950.

97. Ferrante, A., and Rossetti, D.: Aneurin in High Doses in Treatment of Glaucoma, with Particular Reference to the Anticholinesterase Activity, Gior. ital oftal. **4**:25-40, 1951.

98. Obal, A.: Value of Corpus Luteum Hormone in Glaucoma Therapy, Klin. Monatsbl. Augenh. **117**:201-203, 1950; footnote 61a.

99. Blake, E. M.; Fasanella, R. M., and Wong, A. S.: Effect of ACTH in Glaucoma, Am. J. Ophth. **33**:1231-1235, 1950.

IV. Surgical Treatment of Primary Glaucoma

In view of our lack of understanding of the origin of glaucoma, the operative approach to glaucoma must still be utilized in many cases, even though it is in general unsatisfactory. Many of the papers have dealt with the mechanism of action of the various procedures.

A. Fistulizing Operations.—1. Mechanism of Action: Kronfeld and McGarry [5a] report, in an excellent paper, their attempt to determine whether iris inclusion operations are effective through creating new outflow channels for intraocular fluid or whether their primary effect results from a modification of the circulation of the anterior uveal tract, possibly by the inhibition of axon reflexes, as favored by Duke-Elder. They had previously found that eyes with filtering scars of the elevated, polycystic type showed a decided lability of ocular tension in a downward direction. After repeated gentle tonometric determinations, the tension fell more than in normal eyes or in eyes not operated on than in eyes with filtering scars. The authors divided eyes with iridencleisis scars into three types. Type 1 was elevated and polycystic; Type 2 was flat or slightly raised and succulent, while Type 3 showed only the scar of the surgical trauma, or possibly slightly resembled Type 2. In the present paper, eyes with scars of Type 1 or Type 3 were subjected to pressures of 55 gm., applied to the anterior sclera for two minutes by means of a Souter tonometer. The tension of eyes with scars of Type 1 or Type 3 fell much more after compression than did that in control eyes when pressure was applied over the lower limbus. When pressure was applied astride the upper limbus over the scar for the same length of time, the tension dropped considerably less, whereas it was found to be the same at each location in control eyes. The authors, therefore, believe that pressure applied over the scar tends to close off the oblique iridencleisis opening, permitting less fluid to escape. They interpret their findings as strongly supporting the concept that iridencleisis acts as a tension-normalizing operation through the creation of a new drainage channel for intraocular fluid.

Kronfeld,[5b] in another article on the mechanism of filtration operations, in which success or failure in 400 operations was determined by the external appearance of the operative site, gonioscopic examination, and provocative tests, states that the tension was probably lowered through filtration. Gonioscopic examination revealed the site of the trephine hole to be of importance. In his opinion, the center should be placed just in front of Schwalbe's line. A more posterior position endangers obstruction by incarceration of uveal tissue. The tension was successfully controlled in eyes with scars that had polycystic blebs or a flat, succulent appearance which increased on pressure. Somewhat as in his study with McGarry, he found that if the filtration area of an iridencleisis was occluded with a rubber-padded Daviel spoon, pressure did not lower the tension. This was also true in cases in which no gross signs of filtration were seen. He concluded that filtration must be assumed in these cases also.

Coppez and Zanen [100] conclude, as a result of their own observations, based partly upon gonioscopic studies, that both the Elliot trephine procedure and the iridencleisis function by means of fistulization.

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100. Coppez, L., and Zanen, J.: Importance of the Fistula in Elliot's Trephining, Proc. XVI Internat. Cong. Ophthal., London **2**:938-944, 1950.

Van Heuven [101] was also convinced that the corneoscleral trephination was effective through mechanical filtration. Evidence for this was staining in the potassium fluorescinate test, either spontaneously or after pressure upon the globe, enlargement of a cystoid or flattened scar after pressure on the globe, or a greater reduction in tension in the surgically treated eye than in its fellow intact eye following massage. Even if none of these tests are positive and clinical signs of filtration are absent, the scar, in his opinion, may still be filtering.

DeVoe [102] also studied the mode of action in fistulizing operations. As a result of gonioscopic and slit-lamp examination of 91 eyes, he concludes that two-thirds of the eyes examined showed no gross evidence of filtration. Of the remaining one-third, which were considered to be filtering, about one-half showed definite hypotony. In two-thirds of the eyes without obvious filtration, the tension had been controlled. As a result, he states that in most cases of glaucoma success of fistulizing operations is not due to mechanical fistulization but more probably is the result of trauma to the uveal tract and readjustment of the neurovascular system.

François [103] arrived at a similar conclusion when he found, in a study of 30 eyes after corneoscleral trephinations, that the root of the iris was incarcerated in the opening in many of the eyes. He believes, therefore, that the operation is effective, as is iridencleisis, through a neurovascular, rather than a mechanical, mechanism. His observations do not agree with most reports in the American literature.

McNair,[104] on the basis of replies to a questionnaire which he had sent to 125 ophthalmologists, stated that it was the consensus that filtering operations were less successful in Negroes than in white persons because of a greater tendency for the opening to become closed with cicatricial tissue. This would presuppose that the operation was effective through filtration of aqueous. According to this survey, the tendency to scarring was greater with trephination than with iridencleisis, and the latter was therefore favored as the operation of choice in cases of chronic simple glaucoma. Cyclodiathermy was finding increasing favor.

2. Results, Complications and Causes of Failure of Operations for Glaucoma: Numerous papers have appeared in the literature during the past year citing a wide range of statistics on the results of various operations for glaucoma and their indications. Most of this information is already available, and much of it represents differences of opinion, depending on entirely different concepts and criteria.

Lewis,[105] in an excellent paper on the complications of operations for glaucoma, presented an excellent review of the subject of glaucoma surgery in general. Much of the technique is outlined, as are indications for operation in various types of glaucoma. Detailed discussion of this paper is not practical, but the article is one which can be read with profit by anyone interested in glaucoma surgery. The operations considered are iridectomy, corneoscleral trephination, iridencleisis, cyclodialysis, and cyclodiathermy.

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101. Van Heuven, J. A.: Trephining Operations, Am. J. Ophth. **33**:1387-1391, 1950.

102. DeVoe, A. G.: A Gonioscopic Study of Fistulizing Operations, Tr. Am. Ophth. Soc. **48**:118-125, 1950; A. M. A. Arch. Ophth. **46**:504-509 (Nov.) 1951.

103. François, J.: Elliot's Operation Is Only an Incarceration of the Iris or Ciliary Body, Ophthalmologica **121**:1-11, 1951.

104. McNair, S. S.: Chronic Simple Glaucoma in the Negro, Am. J. Ophth. **34**:70-76, 1951.

105. Lewis, P. M.: Glaucoma—Surgical Complications, J. Tennessee M. A. **43**:44-47, 1950.

Chandler [106] contributes an excellent article on malignant glaucoma, the mechanism by which it occurs, and its treatment. He quotes Von Graefe's definition of the condition:

> One sees bad cases in which if the anterior chamber is flat there is a rise in tension during the immediate postoperative period. The iris and lens are in contact with the cornea. The eye begins to tear, there is circumcorneal injection. . . . The patient is aware of great tenderness in the ciliary pain. . . . Visual acuity falls in an alarming fashion. . . . In summary there can be no doubt that through operation a new glaucomatous process is brought about which is unusual only in the continued failure of the anterior chamber to form.

Chandler reports six cases, in four of which the glaucoma followed iridencleisis, and in two, a corneoscleral trephination. He emphasizes that in most of the reported cases if one eye took a malignant postoperative course, the second eye, when operated on, months or years later, did likewise. This occurred in three of Chandler's cases. According to Chandler, it occurs in 2% of cases and is seen only in eyes with a shallow chamber in which the tension is elevated at the time of operation. Chandler states that the essential feature of the condition is forward displacement of the iris-lens diaphragm, completely closing the angle and blocking the wound. The tension remains high, and the eye is lost unless the anterior chamber can be formed. He postulates that there may be an unusually large lens, or a lens disproportionately large in relation to the anterior segment, which may act as a block between the posterior and the anterior chamber. Posterior sclerotomy may be helpful, but it is not effective in all cases. He believes that for posterior sclerotomy to help, the anterior chamber should be filled with air at the same time. He suggests, however, that prompt extraction of the lens appears to offer the best chance of relieving the condition.

Friedenwald,[65] in discussing the causes of failure in operations for glaucoma, states that episcleral and conjunctival scarring plays a large role in bringing about failures in filtration operations. Among the factors which contribute to scarring are excessive trauma in turning the conjunctival flap, postoperative hemorrhage and inflammation, and scarring from previous operations at the same site. He believes that racial factors are important, for it is his impression that episcleral scarring is more marked in the eyes of the Negro than in those of the Caucasian, probably because of their tendency to keloid formation. He mentions the postoperative use of beta radiation to prevent fibroblastic proliferation and postoperative scarring, although possible complications from this type of therapy must be kept in mind.

3. Modifications in Technique: Numerous articles have appeared describing modifications of present-day techniques. A survey of current literature reveals that the corneoscleral trephination and iridencleisis remain the two most popular filtration procedures for the treatment of chronic simple glaucoma. In eyes with narrow angles, the ab externo incision is increasing in popularity for both iridencleisis and iridectomy.

Preziosi [107] (1924) describes a method of performing a fistulizing operation which consists in entering the anterior chamber beneath a conjunctival flap at the limbus by means of a galvanocautery puncture. The procedure is combined with

106. Chandler, P. A.: Malignant Glaucoma, Am. J. Ophth. **34**:993-1000, 1951.

107. Preziosi, C. T.: The Electrocautery in Treatment of Glaucoma, Brit. J. Ophth. **8**:414-417, 1924.

iridectomy in some cases. He reported a summary of 25-years' experience before the International Ophthalmological Congress in 1950,[108] having operated on 665 eyes. Excellent results were claimed in all types of glaucoma, including buphthalmos. The advantages claimed are simplicity of technique, absence of hemorrhage during the operation, little danger of injury to deeper structures, gradual escape of aqueous, and rare late infection. Cardell[108] used the same operation and reported success in 25 of 35 cases, while Néame[109] reported only 4 failures in 17 cases.

Szymanski[110] describes an interesting modification of the Elliot trephination in which he removes only a partial corneoscleral disk at the limbus. A conjunctival flap is first prepared by incision at the limbus, as in peritomy.

Articles on iridencleisis to which the reader is referred are those by Hruby,[111] Purtscher,[112] Scharf,[113] and Sourdille,[114] who discuss their views on points in technique, indications, and results. Sourdille's articles are particularly informative. He emphasizes keeping the surgical trauma to a minimum, a technical point upon which all operators agree.

B. Cyclodiathermy.—1. Results: The literature on cyclodiathermy has increased greatly in volume during the past year. Meesmann,[115] in a paper of some significance, reports an eight-year follow-up study of 102 eyes operated on by the Vogt perforating technique. The operation was judged to be successful in 50%. He also described the use of the Weekers nonperforating method, in which the sclera is cauterized through the conjunctiva 7 mm. from the limbus, and found a comparable percentage of success, although the period of observation was only 3 to 18 months. He believes the operation is indicated, particularly in cases of secondary acute glaucoma, or in other instances in which other operations may be dangerous.

Weekers and Weekers[116] report success in 68% of all cases of chronic simple glaucoma and in 85% of cases in which the initial tension was not over 40 mm. Hg. They also suggest that cyclodiathermy, because of its innocuous nature, should be used upon eyes on which one would hesitate to perform other types of surgery. These included eyes with secondary glaucoma, absolute glaucoma, and advanced glaucoma of any type. The authors are investigating its usefulness in acute glaucoma.

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108. Cardell, J. D. M.: Preziosi's Operation, Proc. Roy. Soc. Med. **43**:815-818, 1950.

109. Néame, H.: Experimental Investigation into Effect of Electrocautery Puncture and Diathermy Puncture (1) in Human Cadaver Liver Tissue, (2) into the Anterior Chamber of the Rabbit Eye: Report on 20 Cases of Preziosi's Operation for Glaucoma, Proc. XVI Internat. Cong. Ophth., London **2**:975-987, 1950.

110. Szymanski, J.: Fistulizing "Half-Elliot" Operation for Glaucoma, Am. J. Ophth. **33**:1601-1602, 1950.

111. Hruby, K.: Iridencleisis with the Knife, Klin. Monatsbl. Augenh. **116**:627-634, 1950.

112. Purtscher, E.: Antiglaucomatous Iridencleisis, von Graefes Arch. Ophth. **150**:358-373, 1950.

113. Scharf, J.: Surgical Treatment of Glaucoma by Diascleral and Subscleral Iridencleisis, Klin. Monatsbl. Augenh. **115**:500-506, 1949.

114. Sourdille, G. P.: Indications and Technique of Iridencleisis, Brit. J. Ophth. **34**:428-434; 435-441, 1950.

115. Meesmann, A.: Criticism of Antiglaucomatous Ignipuncture, Ber. Versamml. deutsch. ophth. Gesellsch. **55**:202-212, 1949.

116. Weekers, L., and Weekers, R.: Scope of Thermometric Retrociliary Diathermy: Non-Penetrating Superficial, Indirect, Non-Bleeding Cyclodiathermy, Proc. XVI Internat. Cong. Ophth., London **2**:950-958, 1950.

2. Modifications in Technique: Bietti [117] describes a technique in which he applied solid carbon dioxide to the ciliary body about 4 mm. from the limbus. The results apparently approached those of nonperforating cyclodiathermy. The author believes that nonperforating cyclodiathermy of some type should be used in cases in which only a temporary lowering of ocular tension is required, as in secondary glaucoma. It can also be used upon eyes in which classic operations have failed to control the tension. Bietti believes that perforating cyclodiathermy, because of the greater incidence of complications, should be reserved for cases in which the nonpenetrating type fails.

The mechanism of action of cyclodiathermy is still being debated. Reiser [118] suggests that it diminishes the production of aqueous humor. De Walsche,[119] in a histologic study of a case of hypertensive uveitis, in which two cyclodiathermy procedures had been performed three years previously, showed atrophy of the uveal tract at the site of the application of the electrode, a finding which might be used to support Reiser's view. Because extensive atrophy occurred, well to the front and back of the coagulated areas, de Walsche agreed that application of the electrode 8 mm. from the limbus, as represented by Weekers, was rational. Reiser, however, believed that aqueous production was inhibited as a result of changes in the nerve pathways leading to the ciliary body, rather than by atrophy, and for that reason he applied electrodes well back from the limbus.

Several other articles have appeared describing techniques directed at cautery of the ciliary nerves or arteries. Arruga [120] expresses the opinion that Weekers' technique is effective through its action upon the ciliary nerves. He therefore directs his cautery to the region of the tendons of the rectus muscles overlying the long ciliary nerves and arteries. He, as did Weekers and associates,[121] applied the electrode 5 to 15 seconds, a longer period than that advocated by most surgeons. Fifteen to 20 applications were made through the conjunctiva about 9 mm. from the limbus.

Acto-Peis,[122] in a different technique, detached the external and internal rectus muscles and made 8 to 10 punctures just back of the insertion, to coagulate the anterior ciliary arteries, and another row of punctures between the insertion and the limbus, to get the posterior ciliary arteries. Kettesy [123] describes a similar method.

C. Seton Operations.—Seton operations are generally considered impractical. It is possible, however, that with the development of more inert substances as implants, antibiotic therapy, and other adjuncts, such as cortisone, to prevent

117. Bietti, G.: Surgical Intervention on the Ciliary Body: New Trends for the Relief of Glaucoma, J. A. M. A. **142**:889-897 (March 25) 1950.

118. Reiser, K. A.: Operative Results Obtained with Diathermy Punctures of the Sclera, Ber. Versamml. deutsch. ophth. Gesellsch. **56**:155-158, 1950.

119. de Walsche, L.: A Histopathological Study of Hypertensive Uveitis Treated by Cyclodiathermy, Bull. Soc. belge ophth. **92**:220-237, 1949.

120. Arruga, H.: Diathermy of Ciliary Body in Treatment of Glaucoma, Arch. Soc. oftal. hispano-am. **10**:224-229, 1950.

121. Weekers, L.; Weekers, R., and Heintz, A.: Conservative Treatment of Absolute Glaucoma, Bull. Soc. belge ophth. **93**:502-507, 1949.

122. Acto-Peis: Angiodiathermy and Its Relation to Glaucoma, Ophthalmologica **120**:325, 1950.

123. Kettesy, A.: Cyclanemization, a New Surgical Procedure for Glaucoma, Ophthalmologica **120**:334-348, 1950.

reaction, the operation may in the future prove of value. Muldoon, Ripple, and Wilder[124] reported clinical and experimental studies using platinum implants. They caused little reaction in rabbit eyes and only slight pathological changes when the implant was placed so that it was not in contact with the ciliary body. In human eyes, fine platinum wire, 0.002 in. in diameter, was inserted at the limbus into a keratome incision made beneath a conjunctival flap. It was placed in such a way that there was no contact with the lens, iris, or ciliary body. Two eyes were followed for two years, during which time the ocular tension was satisfactorily controlled. As a result of this experience, the authors suggest that, although the operation is not recommended to replace other procedures for glaucoma, it might be considered after failure of other types of surgery.

Parry[125] reports a similar technique, using a tubular tantalum drain inserted through a keratome incision beneath a conjunctival flap, so that one end is in the anterior chamber. In the majority of these patients the wound tended to seal off, but he thinks that the operation is of some value in acute glaucoma, secondary glaucoma with high tension, or glaucoma of long duration with very constricted fields. He suggests that, although drainage is frequently not permanent, the tension remains normal for three or four months, after which a more permanent procedure can be carried out, possibly with greater safety. In only 2 of 25 cases did the tension remain normal for more than three or four months.

D. Combined Operations.—Numerous papers reporting a combination of various operative procedures have appeared during the past year. In the past, many combinations of operations have been reported, such as associations of cyclodialysis, iridectomy, cyclodiathermy, and corneoscleral trephination with each other, and even other procedures. Among recent papers are those by Carreras,[126] Roberts,[127] Henderson,[128] Laval,[129] Reichling,[130] Schmoger,[131] Cavka,[132] and Schreck.[133]

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124. Muldoon, W. E.; Ripple, P. H., and Wilder, H. C.: Platinum Implant in Glaucoma Surgery, A. M. A. Arch. Ophth. **45**:666-672 (June) 1951.

125. Parry, T. G. W.: Use of Tantalum Drains in Glaucoma, Brit. J. Ophth. **34**:684-687, 1950.

126. Carreras, D. B.: Combined Operations in Glaucoma, Arch. Soc. oftal hispano-am. **10**:230-248, 1950.

127. Roberts, F. G.: An Operation for Glaucoma, Tr. Ophth. Soc. Australia **9**:227-228, 1949.

128. Henderson, T.: Combined Quadruple Operation for Glaucoma, Tr. Ophth. Soc. U. Kingdom **59**:529-534, 1950.

129. Laval, J.: An Operation for Glaucoma: Goniodialysis with Sclerectomy and Iris Inclusion, J. Internat. Coll. Surgeons **12**:869-872, 1949.

130. Reichling, W.: Methods and Results of Combined Glaucoma Operations, Ber. Versamml. deutsch. ophth. Gesellsch. **55**:196-202, 1949.

131. Schmoger, E.: Results of the Trephine Operation Combined with Cyclodialysis in Cases of Glaucoma, Klin. Monatsbl. Augenh. **117**:598-606, 1950.

132. Cavka, V.: Non-Perforating Cyclodiathermy with Cyclodialysis Circumscripta in Glaucoma, Brit. J. Ophth. **35**:307-312, 1951.

133. Schreck, E.: Cilioanolysis and Ciliocycloanolysis: A New Glaucoma Operation: Intentional Obliteration of Arteria Ciliaris Posterior Longa and Formation of an Iris-Ciliary Body Channel. von Graefes Arch. Ophth. **149**:95-141, 1949.

INFANTILE GLAUCOMA

Interest in infantile glaucoma continues to center largely upon therapy. Evidence is accumulating to show that goniotomy is an effective surgical procedure, although agreement has not been reached that it is the operation of choice. McArevey [134] reported results obtained from operating on 25 eyes with Barkan's technique. The tension was controlled in 21 eyes over follow-up periods of two months to seven years. Two of the failures occurred in eyes in which the disease was advanced. The author emphasizes the ease of performance of the procedure and the fact that it can be repeated. Other operative methods can be used at any time. Three of the eyes required three operations; 7, two operations, and 10, only 1. He emphasized the poor prognosis in advanced cases.

Robertson [135] reports the performance of goniotomy with or without a contact lens but favors omission of its use because it is unwieldy, occupies much of the space of the operative field, makes the puncture more difficult, predisposes to loss of aqueous during the procedure, and requires unnecessary manipulation of the globe. Sugar,[136] in an excellent review of infantile glaucoma, mentions having done goniotomies on the eyes of five infants but is not enthusiastic about the results. He states that if goniotomy succeeds by separating the mesodermal meshwork from the trabeculum, cyclodialysis should be equally effective. Barkan [137] publishes the exact measurements of his goniotomy knife and surgical contact lens, with excellent illustrations.

Weekers and Weekers [138] express the opinion that infantile glaucoma is due to a malformation of the vascular system of the uveal tract, and for that reason they prefer iridencleisis to goniotomy. This line of reasoning is somewhat supported by Joy,[139] who adds a case of naevus flammeus associated with glaucoma to the literature. In this group of cases, at least, the disease seems to be on the basis of a vascular anomaly. In another article, Weekers and Weekers [116] state that the cyclodiathermy done according their technique is most useful in cases of buphthalmos.

Scheie [140] describes a new procedure, termed "goniopuncture," which he developed as a result of experiences with goniotomy. A modified goniotomy knife is carried across the anterior chamber, but, instead of sweeping the knife along the angle, a counterpuncture is made which extends into the subconjunctival space through the trabecular region of the corneoscleral wall. This creates a fistula, which permits subconjunctival drainage and absorption of aqueous. In eyes in which the

134. McArevey, J. B.: Treatment of Congenital Glaucoma, Brit. J. Ophth. **34**:568-573, 1950.

135. Robertson, E. N.: Goniotomy in Congenital Glaucoma, J. Oklahoma M. A. **43**:409, 1950.

136. Sugar, H. S.: The Congenital or Infantile Glaucomas, Am. J. Ophth. **33**:1676-1680, 1950.

137. Barkan, O.: Goniotomy Knife and Surgical Contact Glass, Arch. Ophth. **44**:431-433 (Sept.) 1950.

138. Weekers, L., and Weekers, R.: Pathogenesis of Buphthalmos, Ophthalmologica **120**:285-298, 1950.

139. Joy, H. H.: Nevus Flammeus Associated with Glaucoma, Am. J. Ophth. **33**:1401-1409, 1950.

140. Scheie, H. G.: Goniopuncture—A New Filtering Operation for Glaucoma, Arch. Ophth. **44**:761-782 (Dec.) 1950.

tension has been normalized a persistent hole remains at the site of the puncture, which can be seen by gonioscopic examination. Only minimal diffuse conjunctival edema is present over the area of the globe surmounting the puncture, which is best seen with a slit-lamp microscope. The advantages of the operation are that it is easy to do, causes little trauma to the eye, is followed by few complications, and preserves a round pupil, and that the eye is left relatively undisturbed should future operations be necessary. The procedure is still under evaluation, but it seems to offer promise in infantile glaucoma, and its results with juvenile glaucoma are encouraging. The paper adds fuel to the argument regarding the way in which goniotomy lowers ocular tension. Di Vincentiis, who devised goniotomy, believed that the operation was effective through a débridement of the angle of the anterior chamber, while DeWecker thought that the operation probably lowered tension by means of an internal sclerotomy, possibly with subconjunctival drainage of aqueous. This argument has never been satisfactorily settled, but the fact that goniopuncture controls tension through filtration suggests that microscopic fistulae may be produced by goniotomy.

SECONDARY GLAUCOMA

The literature on secondary glaucoma during the past year has also dealt largely with therapy, and to a less extent with etiology. The mechanism of secondary glaucoma is fairly well understood. There is little debate that both neurovascular and mechanical entities can be of extreme importance, either separately or together, in the same eye. There is sufficient reason to believe that either one alone can cause intractable secondary glaucoma or at other times serve as a contributing factor. Bottoni [141] describes gonioscopic studies on eyes with glaucoma secondary to uveitis; he found the angles of the anterior chamber to be normal, while François [142] found that in certain instances narrowing of the angle was a factor. The effect of inflammatory adhesions in closing off the angle secondary to inflammatory processes is a widely accepted concept.

The effect that the vascular element plays in the tension of inflamed eyes is emphasized by Goodside [143] in an interesting article, in which he reports a patient with chronic simple glaucoma whose tension became normal during attacks of iridocyclitis but was elevated when the eye was quiet. This sequence of events was probably the same as that which causes the occasional hypotony in severely inflamed eyes.

Agreement is becoming more general that surgical intervention should be delayed as long as possible in glaucoma secondary to uveitis. Clark [144] states that operation should be resorted to only after thorough medical treatment has been to no avail. Posner [145] points out that cupping of the disk and loss of field do not occur early in this type of glaucoma, and for that reason operation can be delayed. Clark

141. Bottoni, A.: Alterations of the Iridocorneal Angle in Hypertensive Uveitis, Ann. ottal. e clin. ocul. **77**:84-89, 1951.

142. François, J.: Gonioscopic Studies of Glaucomas Secondary to Uveitis, Ophthalmologica **119**:44-55, 1950.

143. Goodside, V.: Occurrence of Acute Iridocyclitis in Patient Having Chronic Simple Glaucoma, New York J. Med. **50**:455, 1950.

144. Clark, W. B.: Glaucoma Secondary to Uveitis, Am. J. Ophth. **33**:1669-1673, 1950.

145. Posner, A.: Management of Glaucoma in Iridocyclitis, Eye, Ear, Nose & Throat Month. **29**:95-96, 1950.

emphasizes, as did Kalt,[146] that treatment should be directed at the underlying uveitis. For that reason, he believes that atropine is usually indicated, along with a general medical regimen for the treatment of uveitis. François [142] emphasizes that gonioscopy should be done before atropine is instilled because of the danger of superimposing an acute congestive glaucoma if the angle is narrow.

Knighton [147] contributes an excellent article on glaucoma secondary to trauma. He believes that the rise in tension usually results from a disturbance of the local nervous control of the ocular circulation and suggests directing surgery to the causes of the irritation, such as iris adhesions and dislocated lens. He recognizes the importance, however, of obliteration of the filtration angle.

Rychener,[148] in an excellent review on glaucoma of lenticular origin, discusses that associated with intumescent cataract, hypermature Morgagnian cataract, exfoliative cataract, and subluxated lens. He attributes glaucoma secondary to intumescent cataract to mechanical obstruction of the filtration angle due to forward displacement of the anterior portion of the ciliary body and the root of the iris. He believes that combined intracapsular extraction is the procedure of choice, a view which is rapidly becoming widely adopted. Hypermature Morgagnian cataract, he believes, may result from mechanical trauma to the ciliary body and iris root by movement of the nucleus, or irritation may occur from toxic products of the lens. He also advised a cataract extraction. The reviewer fully concurs and advocates the early postoperative use of cortisone to help prevent further reaction to irritative lens material. Irvine and Irvine [149] express the opinion that the increased tension and blockage of the angle in this type of disease may be due to large mononuclear phagocytes which are absorbing lens material. The heavy flare and protein in the aqueous, they think, were due to liquefied lens material, which had passed through a microscopically intact lens capsule.

Rychener believes, as do most people in this country, that exfoliative cataract is due to changes in the angle with obstruction to filtration. He cites Sugar's experience, which agrees with that of this reviewer, that patients with this type of glaucoma invariably show excessive pigment in the trabecular region. Thomassen,[150] however, after examining 57 glaucomatous eyes, found pigmentation of the chamber angle in only 4, and in none of them was there enough to obstruct the passage of aqueous humor. He therefore doubts that capsular exfoliation is the cause of the glaucoma. Weekers and associates [151] concur in this opinion, believing that the disease is really chronic simple glaucoma and should not be classified as secondary in type.

Löhlein [152] presents one of several papers associating glaucoma with the general group of conditions with pigment degeneration and dispersal of the uveal tract.

146. Kalt, M.: Local Treatment in Hypertensive Uveitis, Proc. XVI Internat. Cong. Ophth., London **2**:908-915, 1950.

147. Knighton, W. S.: Glaucoma Secondary to Trauma, Am. J. Ophth. **33**:1673-1675, 1950.

148. Rychener, R. O.: Secondary Glaucoma Due to Cataract, Am. J. Ophth. **33**:1666-1669, 1950.

149. Irvine, A. R., Jr., and Irvine, S. R.: Hypermature Cataract with Glaucoma, Tr. Pacific Coast Oto-Ophth. Soc., p. 89, 1950.

150. Thomassen, T. L.: The So-Called Capsular Glaucoma, Acta ophth. **27**:423-427, 1949.

151. Weekers, L.; Weekers, R., and Dedoyard, J.: Mechanism of Intraocular Hypertension in Capsular Glaucoma, Bull. Soc. belge opht. **95**:383-392, 1950.

152. Löhlein, H.: Knowledge of Essential Progress of Iris Atrophy with Hole Formation and Glaucoma, Klin. Monatsbl. Augenh. **118**:379, 1951.

His patient had essential iris atrophy associated with myotonic muscular dystrophy. He found anterior peripheral synechia at the site of the iris atrophy but questioned whether this might not be the result of the glaucoma rather than the cause. Ojers and Chang [153] reported a case, however, in which they found extensive synechia, progressive in type, at the site of areas of essential iris atrophy with as yet no rise in ocular tension. Their paper suggested that the synechia may be the cause of the iris atrophy, which, as it progresses, conceivably obstructs the filtration angle to cause rise in tension.

McCulloch [154] describes glaucoma associated with irridoschisis, a type of atrophy of the iris in which the stroma appears shredded and broken and pigment is liberated from the pigment epithelium. The author suggests that a similar lesion of the ciliary body might cause an overproduction of aqueous. He describes lesions of the choroid which were interpreted as multiple ruptures. Additional reports of cases of glaucoma associated with retinitis pigmentosa are made by Ciotola,[155] Legroux,[156] and Powell.[157]

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153. Ojers, G. W., and Chang, L. W.: Essential Progressive Atrophy of Iris, Am. J. Ophth. **32**:369-373, 1949.

154. McCulloch, C.: Iridoschisis as a Cause of Glaucoma, Am. J. Ophth. **33**:1398-1400, 1950.

155. Ciotola, D. G.: Relation of Glaucoma to Retinitis Pigmentosa, Boll. ocul. **29**:489, 1950.

156. Legroux, R.: Acute Hypertension Following Placental Implants in a Case of Retinitis Pigmentosa, Bull. Soc. opht. France **77**:46, 1951.

157. Powell, L. S., Jr.: Retinitis Pigmentosa with Bilateral Cataracta Complicata and Bilateral Acute Narrow Angle Glaucoma, Kresge Eye Inst. Bull. **1**:37-38, 1949.

News and Notes

EDITED BY DR. W. L. BENEDICT

SOCIETY NEWS

New Orleans Academy of Ophthalmology.—The newly formed New Orleans Academy of Ophthalmology is planning to hold its first midwinter convention Jan. 2 to 4, 1952. A conference on glaucoma will be the main feature of the meeting. Honor guests will be Sir Stewart Duke-Elder, London, England, and Dr. Paul Chandler, Boston.

The registration fee is $50, which includes associate membership in the New Orleans Academy. Reservations may be obtained by writing to Dr. James H. Allen, Tulane University of Louisiana School of Medicine, 1430 Tulane Avenue, New Orleans 12, or to Dr. Jonas W. Rosenthal, National Bank of Commerce Building, New Orleans.

UNIVERSITY NEWS

The department of ophthalmology of the State University of New York, Medical Center at Syracuse University, will present its second annual postgraduate course on Nov. 30 and Dec. 1, 1951. The following guest speakers will participate: Dr. Derrick Vail, Dr. Frank B. Walsh, Dr. Irving H. Leopold, Dr. Walter S. Duggan, and Mr. Aurel E. Mangold. Inquiries should be addressed to Harold H. Joy, M.D., State University Medical Center, Syracuse, N. Y.

The University of Toronto Faculty of Medicine offers a postgraduate course in ophthalmology extending over three years. The graduate instruction in ophthalmology in the teaching hospitals in Toronto has been coordinated under the direction of the University. The first year on a fellowship the student spends in one of the basic sciences of ophthalmology, and the last two years are spent on the intern service of one or more of the university teaching hospitals.

The fee for instruction is $50 per year, payable to the chief accountant, University of Toronto. An application for appointment may be made to the professor of ophthalmology, University of Toronto Faculty of Medicine. Appointments are made in December, to commence on the following July 1.

GENERAL NEWS

The Research Study Club of Los Angeles announces its 21st annual midwinter Postgraduate Clinical Convention in Ophthalmology and Otolaryngology, Jan. 14 to 25, 1952.

For the otolaryngology group, the guest speakers will include Dr. George Edward Tremble, professor of otolaryngology, University of Montreal Faculty of Medicine, who will present a series of lectures based on his clinical and experimental observations in physiology and diseases of the ear, nose and throat; Dr. Kenneth M. Day, professor of otology, University of Pittsburgh School of Medicine, one of America's foremost teachers in problems related to the ear and its diseases, and Dr. Richard Waldapfel, formerly associate professor at the University of Vienna, who will speak on problems of the nose and throat.

The guest speakers for the ophthalmology section will include Sir Stewart Duke-Elder, director of the Research Institute of Ophthalmology, University of London, England, who will discuss the various aspects of glaucoma, and Dr. Meyer Wiener, emeritus professor of clinical ophthalmology, Washington University School of Medicine, St. Louis, who will present his usual course in Surgery of the Eye. This special course by Dr. Wiener and his associates will be limited to 24 students and will be held from Jan. 18 to 20, 1952.

Transactions of the Ophthalmological Society of the United Kingdom.—The Ophthalmological Society of the United Kingdom holds a considerable stock of certain volumes of the *Transactions* since their first publication. The following years are available: 1903, 1904, 1913, 1914, 1915, 1916, 1925, 1940, 1941, 1942, 1943, 1947, 1948, and 1949.

The council would be glad to present to libraries, medical schools, and hospitals such available volumes as they may desire. No charge will be made other than the cost of packing and postage.

Applications, which will be dealt with in order of receipt, should be addressed to the Honorary Secretary, Ophthalmological Society of the United Kingdom, 45 Lincoln's Inn Fields, London, W.C.2.

PERSONAL NEWS

Appointment of Dr. Rocko M. Fasanella.—Dr. Rocko M. Fasanella has been appointed assistant clinical professor and head of the department of ophthalmology at the Yale University School of Medicine. Dr. Eugene M. Blake is now professor emeritus.

STANDARD NOMENCLATURE OF DISEASES AND OPERATIONS

Fourth Edition

The American Medical Association announces the publication of the Fourth Edition of "Standard Nomenclature of Diseases and Operations." Changes in the new edition have been as much as possible kept to a minimum. Nevertheless, advancing knowledge has made necessary a complete revision of the section on the psychobiologic unit, diseases of the hemic and lymphatic systems, and tumor etiology. A completely new feature of this edition is the inclusion of code numbers of the International Statistical Classification of Diseases, Injuries, and Causes of Death, parenthetically in the body of the book, and a cross reference of International and Standard code numbers as an appendix. The new edition is being published for the Association by The Blakiston Company (Philadelphia) and will be available Jan. 2, 1952.

CORRECTION

In the Annual Review on "Pharmacology and Toxicology," by Dr. Irving H. Leopold, published in the August issue of the ARCHIVES, the sixth sentence of the fourth paragraph on page 173 should read "Bacitracin is very potent against gram-positive organisms, some of which are resistant to penicillin."

Book Reviews

Genetics in Ophthalmology. Arnold Sorsby, Professor in Ophthalmology, Royal College of Surgeons and Royal Eye Hospital, London. Price, $9.50. Pp. 251, with 233 illustrations. Butterworth & Co., Ltd., 4-6 Ball Yard, Temple Bar, London, W. C. 2; C. V. Mosby Company, 3207 Washington Blvd., St. Louis 3, 1951.

The author points out that over the last hundred years the causes of blindness in the world have changed considerably. At the beginning of the last century smallpox was the dominant cause, and during the last 50 yr. various infectious diseases, headed by ophthalmia neonatorum, have played a significant role. With the prevention and cure of the infectious diseases by antibiotics, the congenital, hereditary, and developmental defects have increased in importance, and today if one assesses the blind in terms of years of blindness, rather than in number of blind persons, these defects become enormously important to us. The diseases which depend upon the person's constitution are coming well to the front, and medical genetics is an aspect of the study of constitution.

The author's approach to the subject is best exemplified by quoting a paragraph from the preface:

> Contrary to the widespread belief, medical genetics is not concerned with collecting curious pedigrees of the unconsidered trifles of pathology. At the very least, it is an attempt to elucidate some aspects of the constitutional basis of disease. In some affections the genetic factor is obvious. In others, it can be revealed only by exhaustive investigations aided by an understanding of genetic theory. The genetic anomalies have assumed greater significance with the recognition of modes of inheritance other than the simple autosomal recessives and dominants of the past. Isolated cases of genetic disease are no longer clinical puzzles and unusual modes of inheritance are more readily recognized. A further significant development has been the recognition of the abiotrophic character of many of the genetic anomalies, so that many affections coming on late in life and previously regarded as of environmental origin are now recognized as genetic in type. It is not unlikely that some of the so-called senile degenerations are late abiotrophic manifestations, and evidence is accumulating that senile cataract and primary glaucoma are essentially genetic affections. Indeed, the congenital anomalies and classical forms of abiotrophic defects constitute only a small part of the inherited abnormalities or inherited potentialities towards abnormality of the eye. The scope of ophthalmological genetics is, in fact, very much wider than was suspected by the pioneers of the study, and this enlarged scope has an immediate bearing on the causes of blindness and ocular disease generally, as seen today. And if the scope of ophthalmological genetics has become larger, so has the prospect of the eventual control of the genetically determined affections. The fatalism with which the genetic affections are generally regarded is as unfounded in reason as it is unjustified by achievement already reached.

The book is divided into three sections. Section 1 is a theoretical consideration of modes of inheritance, human pedigrees, and the clinical varieties of genetic disease, with a final chapter on the prospects of control of genetic disease. Section 2 treats of isolated ocular anomalies, with an excellent discussion on refraction and its aberrations. This should be read by all ophthalmologists. Most of us are too deeply steeped in the old point of view of hyperopia and myopia as disease entities. Section 3 deals with generalized disorders having ocular aspects, such as the metabolic disorders and certain systemic entities and syndromes.

There are a good bibliography and an adequate index. This volume is an exceedingly valuable book on genetics as applied to ophthalmology and is equaled only by that of Waardenburg, which, unfortunately for most English-speaking ophthalmologists, is in German.

Specific Dyslexia ("Congenital Word-Blindness"): A Clinical and Genetic Study. By Bertil Hallgren. Translated from the Swedish by Erica Odelberg. Acta psychiat. et neurol. Supplement 65. Pp. 285. Ejnar Munksgaards Forlag, Nørregade 6, Copenhagen K, 1950.

The term "specific dyslexia" is used to denote the disorder commonly known in medical literature as congenital word blindness. During the past few years there have appeared an enormous number of publications dealing with reading disabilities in children. The majority of these are concerned only with reading and do not touch on writing disabilities. In the educational and psychological literature, stress has been laid on the causal significance of secondary factors, but statistical comparisons of groups of children with reading disabilities and control groups have failed to show an association between most of these factors and reading disabilities. The question of the significance of hereditary factors is of considerable theoretical and practical interest, and in the present study the main interest has been focused on the genetic aspects of congenital word blindness.

In the larger cities in Sweden, children with specific dyslexia are registered systematically in the schools. The author had a large clinical material to draw upon from patients sent for examination to the Stockholm Child Guidance Clinic. The greater part of the material considered in this study was taken from the Clinic. In addition, the material was supplemented by children from a Stockholm secondary school, and, as a control group, the nondyslectic classmates of the children from this school were also examined.

The chapters which will be of most interest to ophthalmologists are those dealing with visual defects. The author calls attention to the wide variation in belief in this country regarding the association between reading difficulties and visual defects. In his material, it seemed evident that there was no close correlation between dyslexia and visual defects. In none of the cases in which glasses were prescribed was there any marked improvement in reading and writing from glasses alone. He was unable, in his series, to show any difference between the group of affected and that of unaffected children with regard to the relationship between eye and hand dominance and specific dyslexia. Regarding this factor, however, he admits that the method used for testing eye dominance was not altogether reliable, a factor which diminishes the value of this conclusion. Physical illnesses, neurological disorders, and auditory defects were likewise not found to be of causal significance for dyslexia in any instance. A higher incidence of speech defects was found in the groups of children affected with specific dyslexia than in the groups of unaffected children. The association between speech defects and specific dyslexia was quite evident in the case of boys. While nervous disorders were commoner among children affected with specific dyslexia, the study failed to show any association between mental subnormality and specific dyslexia. The genetic statistical analysis showed that specific dyslexia follows a monohybrid autosomal dominant mode of inheritance, in Groups I and II of the present series the manifestation being practically complete. In some of the families in Group III the mode of inheritance is presumably also a monohybrid autosomal dominant.

This monograph should be of interest to all who are concerned with children suffering from reading difficulties.

Surgery of the Oblique Muscles of the Eye. By Walter H. Fink, M.D. Price, $8.75. Pp. 350, with 93 illustrations. C. V. Mosby Company, 3207 Washington Blvd., St. Louis 3, 1951.

This volume on the oblique muscles is a comprehensive study of this subject, presented in a most intriguing manner. It is divided into two parts, the first 140 pages being devoted to anatomy, which is covered in great detail and fully illustrated with line drawings and photographs of actual dissections. These reproductions of

the author's anatomical dissections portray in a minute manner the intricacies of the relationships of these muscles. They give the reader a clear picture of the structures to be encountered in operating upon the oblique muscles, for particular attention is directed to the surgical anatomy.

In the second part the author, in his full discussion on the physiology of the oblique muscles, quotes largely from the writings of others and thus adds but little to our knowledge. The diagnosis of the defects of these muscles is covered in a manner that will not prove very helpful to the student, for it lacks clarity and concreteness. In his discussion on the surgical indications there are also full quotations from the literature, but he correctly summarizes his recommendations. The surgical techniques are beautifully illustrated and form an important part of this text.

The printing is excellent; all the drawings are well reproduced, and the format of the entire book is extremely pleasing. This volume should be of great help to the ophthalmic surgeon, because it clearly visualizes for him the anatomy and surgical treatment of these muscles.

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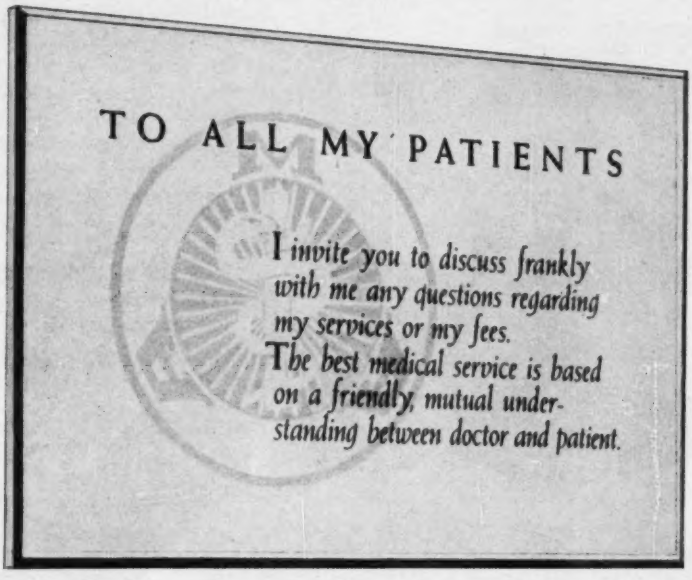
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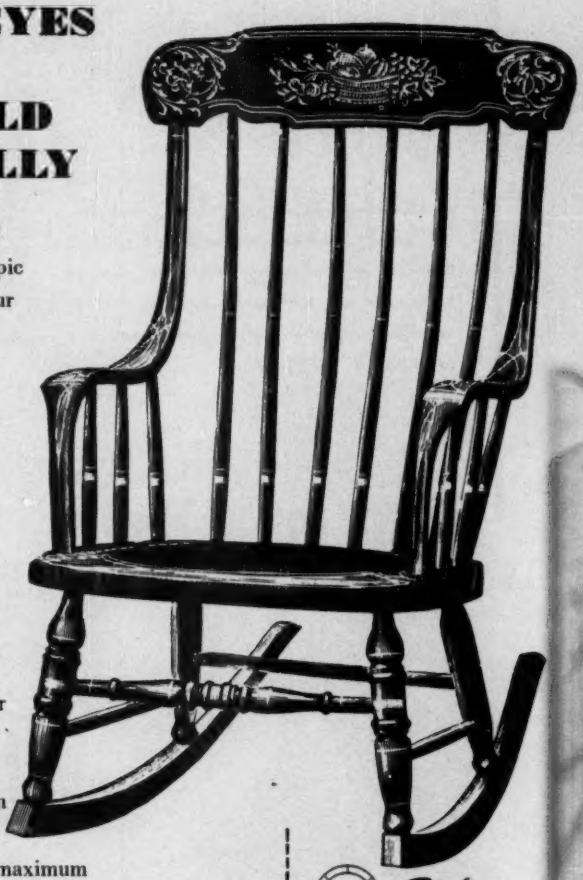
HELPING EYES *to* GROW OLD GRATEFULLY



Comfort counts with presbyopes! Anything you add to the presbyopic Rx for extra comfort adds to your professional prestige.

Every pair of (presbyopic) eyes is different — some eyes can take it, some *cannot!*

Absorptive lenses are different, too — only true Soft-Lite passes the Comparator Test in which ordinary tints turn dark. Light-sensitive elderly eyes grow old gratefully when the comfort of Soft-Lite is specified on bifocal or trifocal prescriptions. Surrounding excess light is absorbed — while full transmission at the near point is provided through the white segments. For maximum efficiency in presbyopic cases, specify Soft-Lite!

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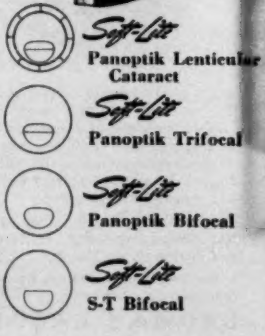
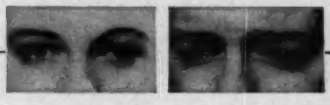


some eyes can take it

...some eyes cannot!



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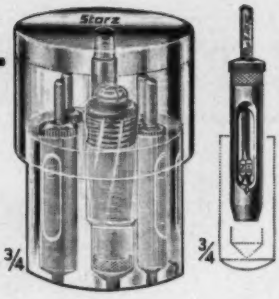

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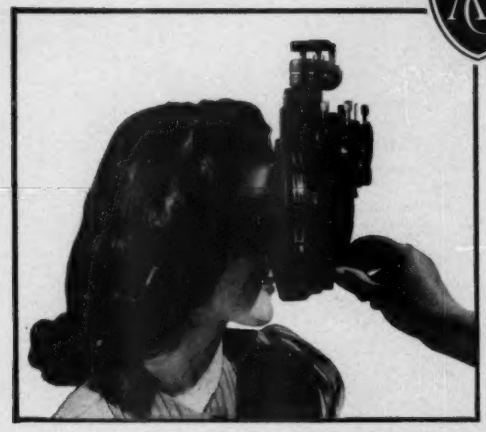
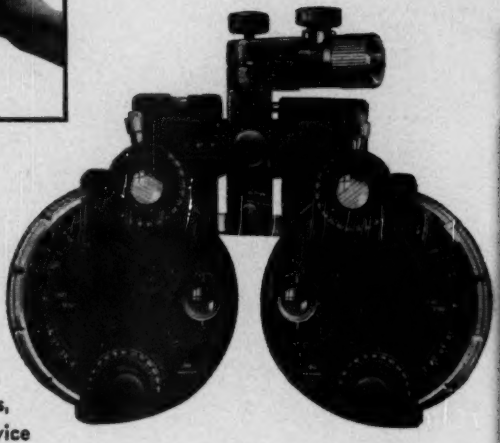


590

ADDITIVE PHOROPTOR



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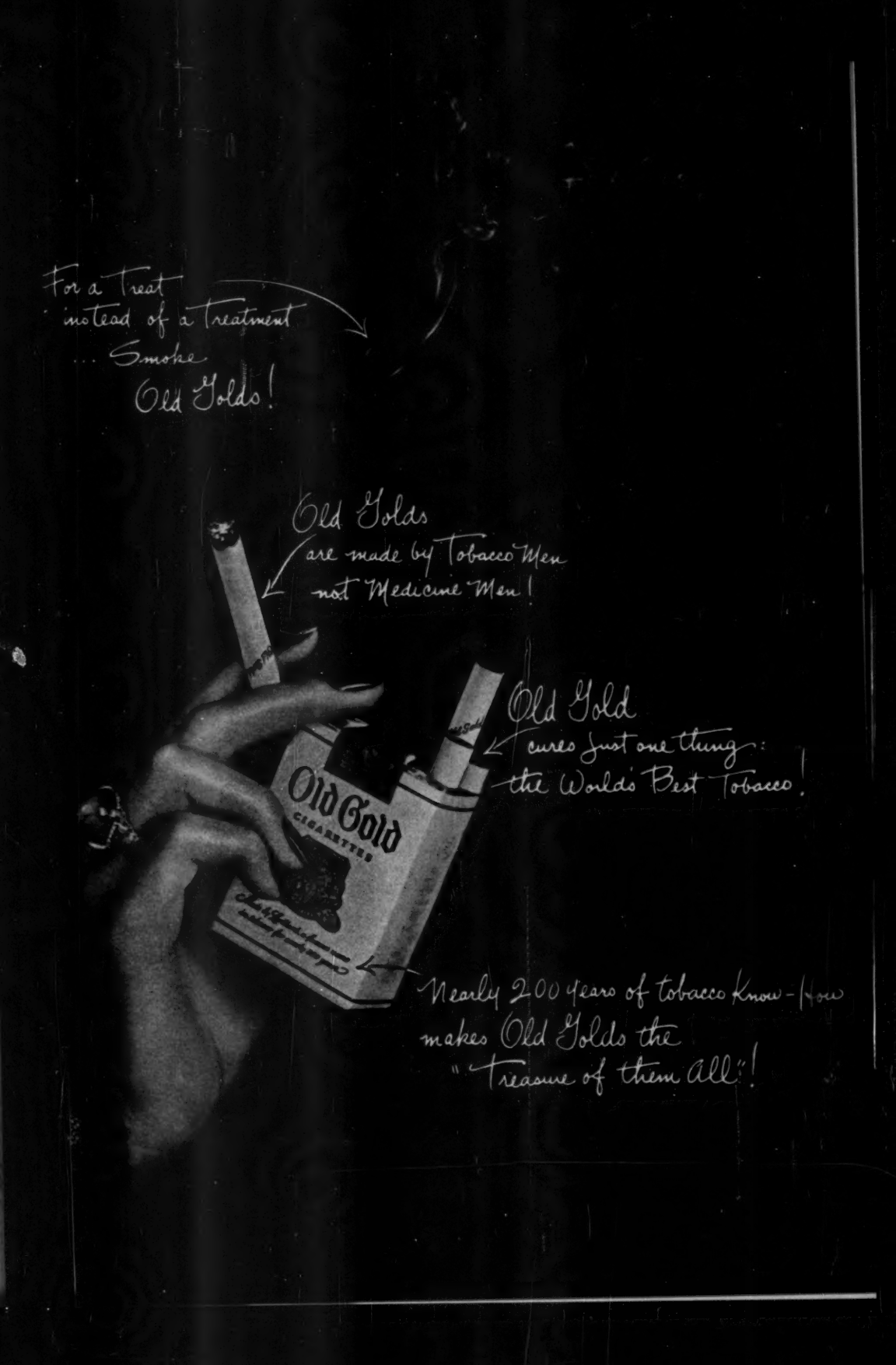
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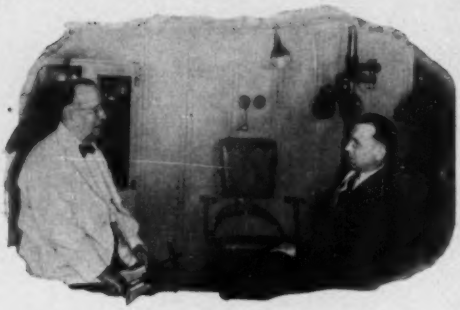

"What's on your mind, Doctor Bob?"

"It's a patient of mine, Dr. Richards—a 22 year old girl working in a factory, welding electrical connections.

"When she first came into my office, her spoilage and rejections were running too high in the afternoon and she was afraid of losing her job. Her eyes felt tired and she got sleepy.

"She accepted a plus 0.50 O.U. for distance but that didn't help her on the job."

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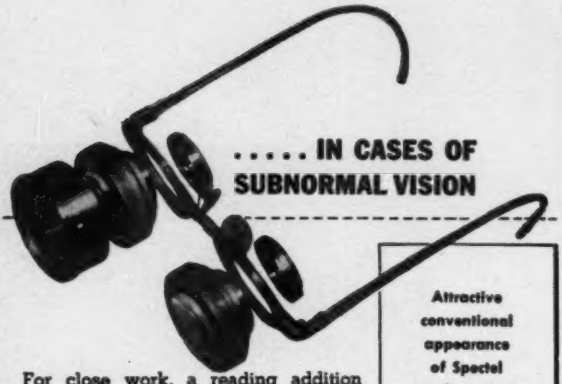

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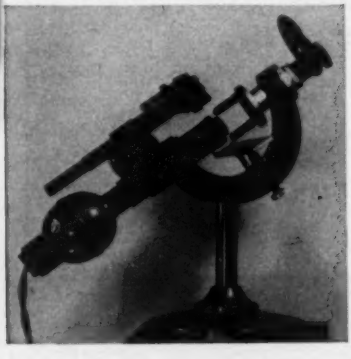

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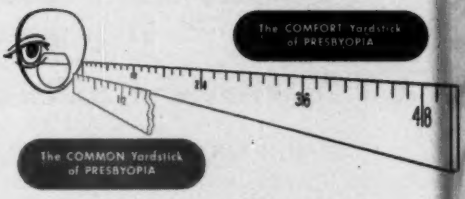

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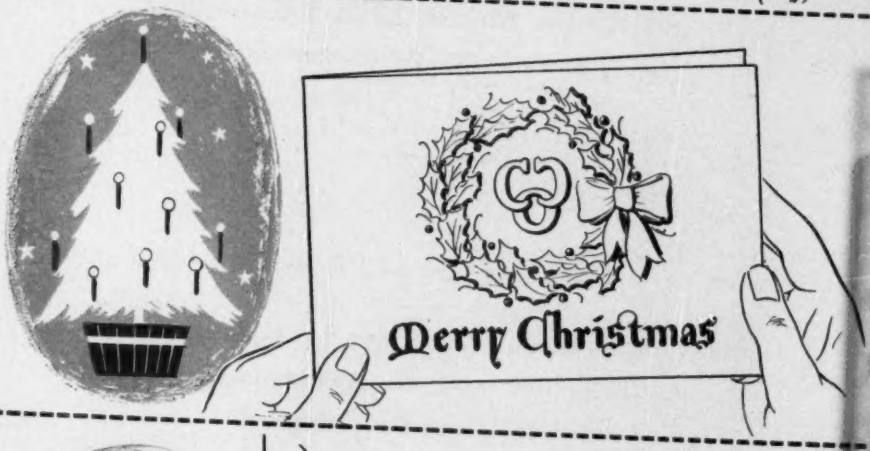
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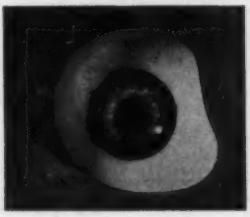

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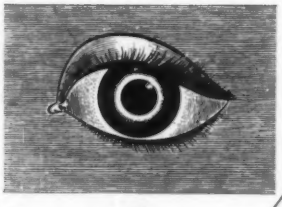

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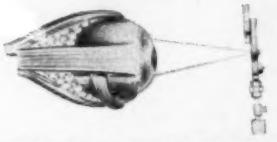

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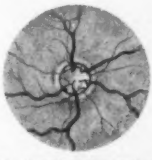

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